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PHYSICAL ANALYSIS IN THE ADOLESCENT PROBLEM *

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THE BIOLOGIC SIGNIFICANCE OF ADOLESCENCE

"Algebraic symbols," says a schoolboy's essay, "are used when you don't know what you are talking about." And surely adolescence is that period of life concerning which, figuratively speaking, one might most readily be excused for employing algebraic symbols.

It is natural to associate adolescence with sex, for the sex features are certainly the most obtrusive characteristics of the period, but actually the term is one of the happiest and most descriptive of the labels applied by science to the phenomena of growth. Its implication is exactly expressed by its etymology. Adolescence is merely the inception of adulthood. In the beginning nature decides whether an organism is to be built on male or on female lines, but it is obvious that before that organism can stand the strain of reproduction other aspects of its development must receive attention. The reproductive function presupposes an organism substantially fully developed. Hence growth and adaptation to the conditions of life must be completed before fulfilment of nature's chief aim. Consequently, although the general broad lines of sexual development were established very early in the process, the reproductive organs lie fallow for a long period during which growth of body and adaptation of response are developed before nature returns to the completion of her task. It is because the technical plan on which the organism is prepared for ultimate supreme usefulness is so obscure that the problem of adolescence is shrouded in mystery. And it is precisely because a physical approach to the problem throws the technical plan into clear relief that this physical approach becomes so valuable. It enables one to grasp more readily the real significance of anomalies and variation by which their very multitude and apparent disorderliness crowd the mind and dull the understanding. The variable date of onset and distressingly erratic sequence of signs, whether physical or mental, appear to offer no clues to the manner or method of preparation for adulthood. But in this composite phenomenon of adolescence, as in so

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many features of human life, a preliminary study of the primates gives the first real indication of solution.

PRIMATE DEVELOPMENT

The extraordinary rapidity with which all mammals below primates reach bodily maturity and reproductive power is a marked characteristic of their life history. In less than two years even the large breeds of dogs are fully matured. Sheep reach adulthood in less than three years; lambs of less than a year will become pregnant if not segregated. A horse or a cow, in spite of large bulk, is adult in four years.

In contrast with this rapidity is the relative tardiness of primate development. Small monkeys take more than four years to reach reproductive potency and are not fully adult until between 5 and 6 years old. Actual bulk is of secondary significance. Even the large anthropoids mature in but little more time than that taken by macaques to reach adulthood. It is not necessary to pause over the lower primates, for their developmental history follows, in the main, the general lines observable in anthropoids.

The chimpanzee weighs about 4 pounds (1.8 Kg.) at birth, but by 7 years the male has reached a weight of 140 pounds (63.5 Kg.) and thereafter continues to increase moderately in bulk to 150 pounds (68 Kg.) or more. The increase in size during these seven years is not an even progress. At the end of the first six months the animal has reached a weight of 8 pounds (3.6 Kg.) or more, the human weight at birth. At the end of two years the animal has overtaken the growth of a human child; both weigh about 28 pounds (12.7 Kg.). By this date the velocity of developmental growth in the chimpanzee has become quite rapid. By its third birthday it has attained the weight reached by a child of 5 years. Thereafter there is less obtrusive progress until the ape's fifth birthday, but between the fifth and sixth birthdays a marked increase in velocity occurs. Dimensions and weight are doubled during this twelve month period, so that by the sixth birthday the animal has attained the stage of development attained by a child at 12½ years. By its seventh birthday, it is at the beginning of maturity corresponding to a youth of 19.

It is not absolute weight but relative velocity of increase which is the significant indicator of progress. The milk teeth are all in place at the end of twelve months instead of the thirty months required by children to complete the deciduous dentition. The first permanent molar erupts soon after the third birthday and the central permanent incisors about the fourth. Then follow lateral incisors, premolars and second molars in relatively rapid succession so that all are in place about

the sixth birthday. Indeed, in the orang-utan, they may all be erupting together.[1]

It is this rapid completion of the permanent dentition, excepting the third molar, which draws attention most strikingly to the distinctive feature in anthropoid development. Within about a year of the eruption of these successive teeth the third molar comes into place. Thus a period of about two years carries the anthropoid from the sixth to the nineteenth year stage of human development. There is no long drawn out period of adolescence in the anthropoid. Adolescence is a specific feature of human life. It is therefore a relatively recent acquirement.

Now it would not obviously be more difficult to construct a man than to construct a gorilla of far greater bulk. Yet the gorilla's body is substantially completed in six years, whereas the same process in man requires twenty. There is something peculiar, apparently, in man's development, not necessarily related to bodily perfection, which requires this long period of developmental growth. One may brush to one side any speculations on this problem and merely note the advantage of this delay in the maintenance of a plastic state for accumulation and registration of experience before the human organism crystallizes out its character.

THE MEANING OF ADOLESCENCE

Whether human adolescence is even now elongating in years is not known, and indeed it is not important for the present purpose. But one would be justified in claiming, on the basis of general biologic observation, that what nature does well, she does quickly. This slowing down of the rate of maturation in human beings is fraught with certain difficulties. Hence, in a general way, the problems of adolescence are probably related to the fact that the process of adolescence is spread out over a long period of time. One does not observe irregularities or disorder in the process of anthropoid adolescence, because in these animals there is no time for disorder to make its presence felt.

On the other hand, the rapid acquirement of adult characters in so short a time puts a considerable strain on the anthropoid so that the transient period of adolescence is dangerous to life itself. This is a time of heavy mortality among apes in general. They sicken without apparent cause. But if they survive this lethal period they are apt to

1. It is not yet settled among those who have kept chimpanzees in captivity whether the great spurt in developmental growth occurs between the fourth and sixth or between the fifth and seventh birthdays. The latter view is taken here and is that of Professor Yerkes. Dr. Noback, however, believes the spurt may occur between the fourth and sixth birthdays. The important fact is that the entire progress is completed in two years. Many facts are still in doubt about the natural history of the anthropoids. Even the weight of the chimpanzee at birth is not yet known with certainty but it is near 4 pounds.

become sturdy, robust animals. In man, on the contrary, the adolescent period has the lightest mortality in the entire life span. Lengthened human adolescence provides many difficult problems, but it probably conserves life.

After all, this period of human development which has become so elongated that it extends from the sixth to the twentieth birthday is the period on which one chiefly depends for training to meet the circumstances of human existence. It is not physical growth that dominates the school period but the transformation of capacity by training into ability. This, one may say, is a feature of mental, rather than of physical, development. It is bound up more with the brain than with the body.

The tempo of the development of the brain is vastly different from that of the body. At birth, the human brain is but one fifth of its adult bulk. At the end of two years it is already three-quarters and by the sixth birthday it is five-sixths its adult size. At the beginning of specifically attenuated human development, the capacity of the brain is almost adult. Thereafter the play of experience transforms that capacity into ability. For this training man has fourteen years, namely, from the sixth to the twentieth birthday, in place of the two years of the anthropoid. If a chimpanzee could go to school he would scarcely have accommodated himself to school environment before his two years would be up and his character would be crystallized in maturity.

Whatever, then, is the meaning of adolescence in detail, it is apparent that one will not err, however dim the present understanding, in groping for its general significance among the subtleties of adaptation to human tasks and responsibilities, a mental rather than a physical complexity.

THE CHARACTER OF ADOLESCENT GROWTH

The character of adolescent developmental growth presents no special features beyond those inseparable from the blossoming of sex. It is true that special hazards arise from the altered character of growth, from the readjustment of bodily functions, and from psychic, emotional and social readaptation. The occurrence of thyroid dysfunction, of increased susceptibility to fatigue, of tuberculosis, the lighting up of old infections and aggravation of cardiac disease are common accompaniments of this period. They enhance the difficulties consequent on variation in type and date of manifestation of the gonadal change which itself is all too subject to disorder. But these are merely the complications, present in less aggravated form, of those dangers which make this period hazardous to health in the anthropoid. The dangers become reduced to difficulties because of human adaptation.

Actually there is no even curve of developmental growth in the child. Evenness of curve is a figment of the average from which statistical

analysis has stripped all evidence of individual character. On the average, there is a spurt of growth soon after the sixth birthday, earlier in girls than in boys, but this spurt is not maintained, and by the ninth birthday both sexes have again reached an approximately common level. Between the tenth and twelfth birthdays, again earlier in girls than in boys, occurs a second spurt by which progress is carried toward maturity. The rapidity of this progress dwindles so that by the sixteenth or seventeenth birthday the drop in acceleration is marked indeed.

Superposition of individual curves of developmental growth on this mediocre average demonstrates that it bears no relation whatever to the phenomena as seen in children who illustrate growth in apparently a most erratic manner. The grade school spurt and the junior high spurt are present in all children. They occur also in anthropoids. But in man and ape alike their exact location on the curve of growth is determined by the interplay of factors obscure at present and differing in their final effect from individual to individual.

THE SKELETAL REGISTER

Researches associated with the names of Rotch, Pryor and others have compelled attention to the manifestation of developmental growth as indicated in the skeleton. That these investigations should form merely the basis for more elaborate study and should leave the mind in grave doubt regarding the real value of the method is no discredit to them. With the material and evidence at the disposal of previous investigators, handicapped by incompleteness of the necessary data, it is remarkable that they should have succeeded so well. No study of developmental growth is adequate unless it takes into account the misadventures in health and in socio-economic conditions which fall to the lot of human beings. To rest the case on inherent variability of human growth is but to bury the problem among the sunken folds of a disused mentality. One must probe deeper now that there is active cooperation from the social services.

Epiphyseal union, which is a characteristic feature of the adolescent skeleton, is indeed subject to considerable variation in date, but this variation is the expression of specific interplay of factors controlling progress toward maturity. It is but the evident end-result attained by different combinations, the identification of which calls for further exploration of the problem presented by each child.

Whatever the date of epiphyseal union, whether it is retarded below or accelerated beyond the average age, the order of union in the several epiphyses is always the same. Further, this order is substantially the same throughout the primates including man. Once the average date is determined, the constancy in order of union gives a measure of developmental progress and enables one to define the physical status of

any child in terms of developmental years. This is a very significant addition to analytic investigation. It gives an estimate of the handicap. If, for example, a child suffering from thyroid deficiency or diabetes shows an epiphyseal union pattern five years below that of the average child of identical age, we in these laboratories who have been interested in the adolescent problem have measured the handicap. If, after suitable treatment with thyroid or insulin the epiphyseal union pattern rapidly approaches that characteristic of the healthy child of identical age, we have measured the efficacy of our treatment.

But the problems presented by all children are not thus easily disposed of. There are many children in whom the factors inducing

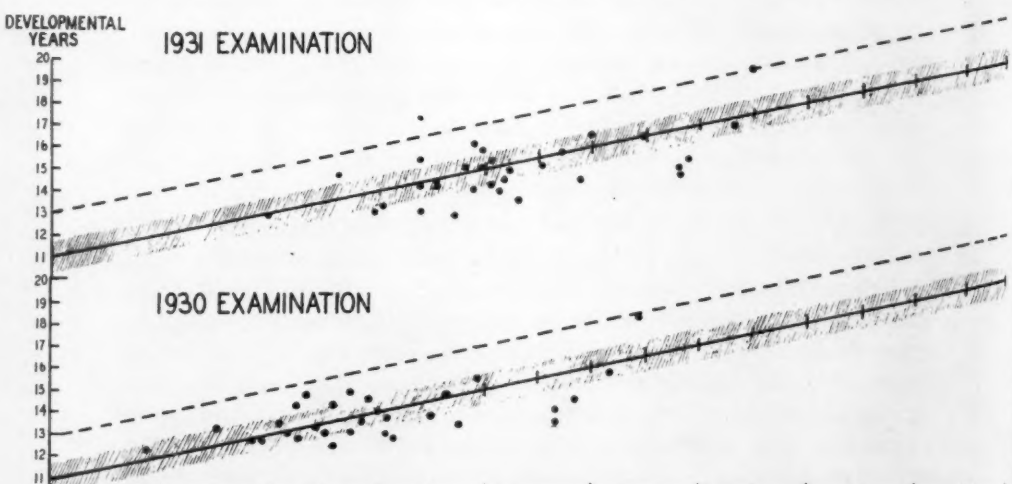

Chart 1.—Skeletal development levels in a contest of boys chosen by the schools for their superior physical development and qualities of leadership and personality. The hatched belt about the mean diagonal represents average development as identified by roentgenograms of the skeleton. Its limits are three times the standard deviation of three months, namely, nine months above and below the mean. The broken diagonal indicates the distance above the mediocre average which represents the superior child. The boys were examined for progress a year later. Note that most are mediocre in development and contrast this with the result found in girls.

handicaps of development are much more obscure. A considerable proportion of the entering class of youths into the university shows retardations in adolescent development measured by the date of appearance of beard and of breaking of the voice. These instances of superficial defect are accompanied by deeper registration in retardation of skeletal maturity. And the developmental age of the epiphyseal union pattern gives

a time-measure of the defect. The more extreme instances also demonstrate a lowering of metabolic rate.

It is a curious but significant finding that adolescents of good stock, of good nurture and of economically privileged families show a union-pattern approximately, on the average, nine months ahead of the mean date, as evidenced by random samples from the Cleveland Public Schools. Very superior types of children, who have escaped or successfully overcome their childhood handicaps, are two, or even two and a half, years ahead of the random samples. These children are also superior in a corresponding degree in height, weight and mental age.

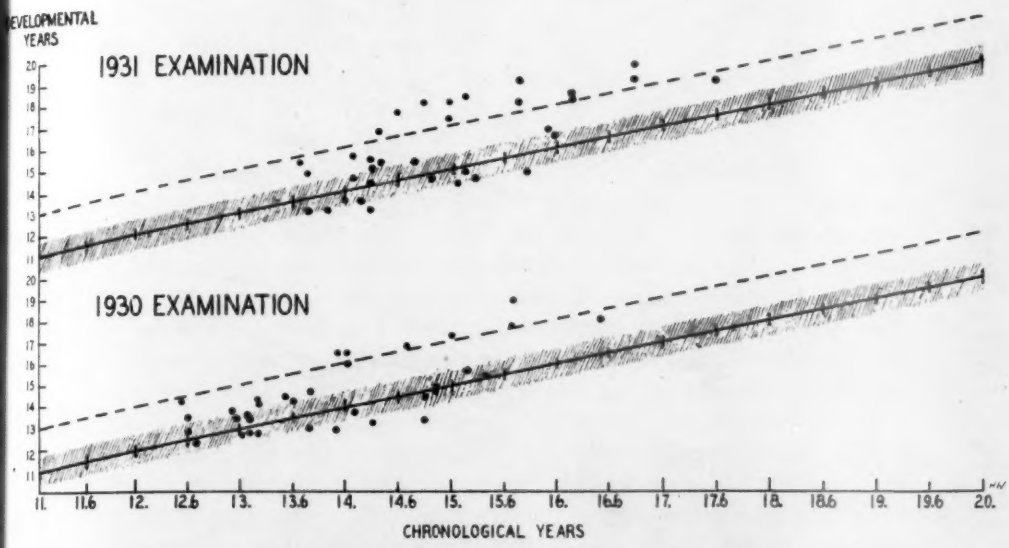

Chart 2.—Skeletal development in a contest of girls chosen by the schools on the same basis as the boys. Note the relatively large number of girls clustering around the broken diagonal. The increased number in 1931 is a measure of developmental progress. The graph illustrates vividly the velocity of progress of girls at these ages contrasted with the slow velocity in the boys.

One might term this leeway of two developmental years the credit balance in the bank of nature. It is the physical expression of that vitality given one to draw on in time of emergency. No child passes through his developmental stages without delay, interruption or, all too often, more or less permanent inhibition of developmental growth. And the end-result is registered in his very bones.

That this physical registration is actually a dependable quantitative measure is indicated by its relationship not only to dimensions and mental development but to other features such as inception or menstruation. The girls who are superior on the foregoing standards menstruate

early. But since developmental growth occurs in spurts, one may not agree that a girl of 15 years who shows a developmental age of 17 commenced to menstruate at 11. The spurt may have started not at 11 but at 13. In other words, a single examination gives a definition of status not a measure of progress. For that, serial examination is needed.

The physical approach to problems of adolescence gives a new and quantitative measure of actual physical status. It is not an academic finding but an exceedingly significant indicator of constitutional health or defect and throws the first clear light into an obscure corner of pediatrics.

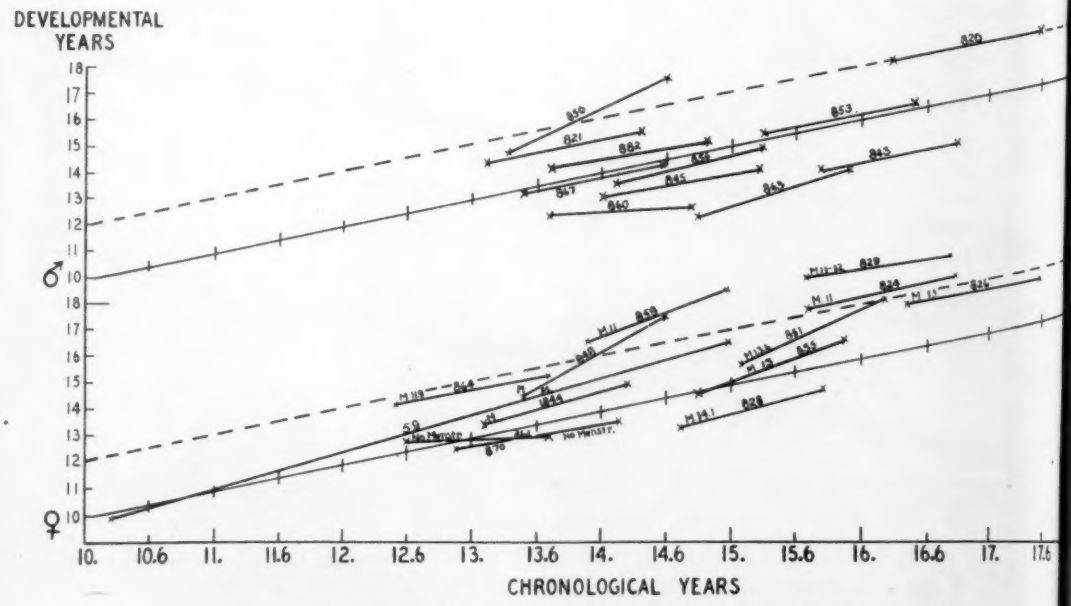

Chart 3.—Graph illustrating developmental progress of a random sample of the children studied. Note the spurts of development in nos. 850 and 859. *M* in the girls denotes date of menstruation, but where it cannot be inserted at the exact chronological date, the date of onset is noted. No. 59 illustrates the steady improvement in physical development of one girl under observation for five years.

THE MENTAL RESPONSE

Looking into the future, I believe that this method of physical approach will prove to be applicable to problems of the mind as well as to those of the body. It is only recently that the developing morphologic pattern of the brain and the expanding cranium during childhood have begun to make their impress on consciousness. I can do no more than allude to the probable great significance of further studies on the developing cerebrum of the child. At the moment the problem can be

roughly sketched. Localization of function within the cerebrum is established beyond a doubt, but the mind acts as a unit. This whole-mindedness is the mental counterpart of physical coordination in bodily responses. The body reacts as a unit in terms of its training, the mind in terms of its experience. A defect in mental response, like a physical infirmity, is due to one of three causes: First, the actual brain substance may be destroyed or inhibited in development as in monoplegia or congenital idiocy. Second, there may be an actual interruption in association tracts as in certain visual defects, in disabilities of reading or speech. Third, there may be a simple evanescent or purely temporary interference with general mental coordination, a kind of blanket of fog obscuring the response pattern as illustrated in change of personality, defect in judgment, reduced power of concentration, inability to grasp the detailed sequence of a story or argument, or even no more than a nominal aphasia. It is the third of these with which one is specially concerned in the mental growth of adolescence.

Good endowment at birth, good nurture, adequate control of infection and other risks of childhood must be supplemented with appropriate training if the child is to develop a healthy ability to cope with the tasks of life. Since the cerebrum is substantially adult at 6 years, it follows that the period of what may be termed gross mental development terminates about that date. Thereafter mental development takes on a different character. One might liken the distinction between the new and the former mental development to that between epicritic and protopathic sensations. It is the finer discrimination of judgment trained by experience which thenceforward dominates the mental growth. It is subject to interference by influences which themselves develop out of the functional activity of a human organism. During the adolescent period, the developing sex glands are associated with readaptations in mental response. The child brings to bear on events and experiences a quickened and altered sensitivity. Even sentimentality, the most unlikable of all adolescent features, is merely the grease which lubricates interaction of reason and passion.

Just as there is a credit physical balance for each one of us in the bank of nature so, I imagine, there is a credit mental balance. And the proper interpretation of a high intelligence quotient or mental age would seem to be an expression of the state of this credit balance. An analysis of physical development on the lines indicated in this essay permits one to assess the working in the mental pattern of those subtle influences which are inseparable from the stage of general bodily development.

If a child has a physical development out of tune with his years, he can usually effect an adjustment provided his mental development is within normal range. It is the children of aberrant intelligence quotient who have their difficulties enhanced by physical disharmonies.

THE PEDIATRICIAN'S RESPONSIBILITY

As adults, pediatricians look on the toils in which adolescence finds itself much as Henchard did in "The Mayor of Casterbridge." Hardy said:

> Henchard found himself again on the precise standing which he had occupied five-and-twenty years before. Externally there was nothing to hinder his making another start on the upward slope, and by his new lights achieving higher things than his soul in its half-formed state had been able to accomplish. But the ingenious machinery contrived by the Gods for reducing human possibilities of amelioration to a minimum—which arranges that wisdom to do shall come pari passu with the departure of zest for doing—stood in the way of all that. He had no wish to make an arena a second time of a world that had become a mere painted scene to him.

To the adolescent the world is very real indeed. Separated from his parents by those twenty-five years, palpitating with eagerness and driven by internal urges of which he cannot understand the full significance, he rebels against sinking from the importance of childhood into the insignificance of adult age. Three things are to him of utmost importance: the need for sympathetic understanding or affection, the desire to excel or vocational guidance and the craving to escape for a while the grim realities of life, some temporary shelter from the exhaustion of training.

It is here that play fulfils its most significant rôle. The healthy effect of organized activity among his fellows brings with it experience and adjustment without which he cannot succeed to his own satisfaction. He is not content to ape; he wants to monkey! The real dangers in adolescence result more from his relationship to his seniors than to his equals. Hence I would submit that the adolescent child falls within the purview of the pediatrician rather than of the internist. The former is accustomed to deal with the growing human organism and should, by training, be more appreciative than the internist of the expanding horizon of the young, expanding, through their efforts, beyond the limits of his parents' thought.

But, if the adolescent is appropriated by the pediatrician, the children's hospitals must be the scene of many changes, though only such as would bring the pediatrician's hospital responsibilities into line with his private practice. It is not too severe an overturning of the present schemes to provide wards for segregation of the sexes in the adolescent age or to pin on the hospitals an enlargement of the social services to undertake the necessary educational facilities.

There is but little information, as yet, on that large area of the cerebrum which lies behind the kinesthetic center, but evidence slowly accumulating in our laboratory testifies to its importance during this period of adolescence. We know that a tumor of the parietal area results

in astereognosis, which means, of course, the loss of all that experience teaches. Refined methods of analysis demonstrate that during the school period, especially grade and senior high school stages, the cranium overlying the parietal area is the actively growing part. In this growth the lambdoid suture plays an all important part. Adolescence is childhood, though on the threshold of maturity, and as such is the natural responsibility of the pediatrician.

SIGNALS OF ADOLESCENCE

In the past understanding of adolescence has been greatly handicapped by lack of critical methods of approach. Generalizations fail when one is face to face with the problem presented by the individual child. But in these days of positive health movements one may hope to see the serial examination of the well child become a part of the physician's regular duty. And in this serial examination I am confident that the recent work undertaken by the Brush Foundation has much of real assistance to offer. New standards of growth and measures of development are necessary. The body itself can guide one in estimating with scientific precision the progress toward maturity.

Awakening of the sex glands produces a profound effect on the body. I am not just now concerned with the amount or type of food best suited to adolescent growth. We have made many studies on groups of growing children from different social strata in Cleveland. Nurture indeed has its influence, and the children of the economically privileged classes show clearly a growth superior to and a development advanced beyond those of the underprivileged. Boys of the latter class average fourteen years and three months as the date of union in the primary elements of the os innominatum at the acetabulum. Boys of the former class average thirteen years and nine months.

Just before the adolescent spurt in stature both in boys and in girls we find a sudden rapid increase in pelvic breadth as if the booster station of the sex glands were affecting local development before it spreads its influence over the entire organism. In girls, on the average, this increase in pelvic breadth, measured by the intercristal diameter, occurs just before the thirteenth birthday, though there are many trailers who do not show this indication till two years later. In boys, on the average, it occurs just after the fourteenth birthday, though here again there are laggard individuals.

It has been said that girls commence to menstruate earlier than they used to. I do not think this is wholly due to improvement in nurture but to the maintenance, by better health conditions, of a greater credit balance in nature's bank. Progress toward maturity suffers less interruption than it formerly did. Health contests in Cleveland have enabled us to study the progress in growth and development of the most superior

and healthiest types of children. And we have been able, by our skeletal measures, to plot velocities of maturation in the adolescent period. I am not about to weary you with an exposition of our results. I wish merely to emphasize the conviction that the methods I have outlined give us an opportunity for precision of analysis new to medical study.

The laggard progress of many boys is not to be attributed to an inherent sex difference, for analysis of the Cleveland records shows no clear sex differences in progress to maturity, but, throughout childhood, there is the same tendency as seen during adolescence, for a larger proportion of boys than of girls to show defects of a temporary nature in growth and development velocities. Similar results occur in our monkey colony: we have greater difficulty in rearing our male monkeys which are specially susceptible to disorders of nutrition involving bodily growth and skeletal development. An analogous difference is observed in the scholastic records of Cleveland children. Superintendent Lake reported that in 40,000 records of children between 12 and 18 years, the boys who failed to be promoted outnumber the girls by more than two to one. And the majority of these failures are found in the junior high schools at 12, 13 and 14 years. We have made comparative records of growth and of skeletal development of the junior high school children of Cleveland and of the children of equal age, who, on account of scholastic dulness, are held back in the grade school. These children are almost invariably retarded in growth and in skeletal development as well as in mental ability. Even on entrance into the university many freshmen show a similar laggard condition, but it remains for the future to segregate among these the temporarily retarded and the more profound disturbances of development. There is no necessary correlation between low mentality and defective physical development, but there is a predisposition to association.

THE ADOLESCENT PERSONALITY

Adolescence, though vastly important because it is a period of adaptation to the conditions of adult life and culture, presents no really specific problem. It is the final stage of childhood and can be studied in its mental and physical aspects with the same precision as the early reaches of infancy. Its problems are bound up in our cultural complexes. Margaret Mead, in Samoa where there are no sex repressions in a safe geographical and social community, found that there is no adolescence crisis among the girls. Now the social ways of one community are never the social ways of another. A strong personality can be developed only by learning to adjust itself to the tasks of life. It is here that play becomes of paramount importance. Play is essential for physical growth and development. It is essential to those refinements of training which are defined as coordination and development of behavior patterns. It

has a tremendous influence on personality because it trains the child to adjust himself to his social environment among children of his own age. And it establishes patterns of behavior which he can confidently carry with him into adult life.

The pediatrician can never hope to succeed in his study of adolescence except by feeling his way steadily from the physical aspect on which he has some secure basis of understanding to the less explored regions of the mind and of the spirit.

A thought is a real thing; words are but its raiment. The adolescent is in the position of having the thought but neither the language to express it nor the experience to understand it. The whole underlying ferment in adolescence is beautifully phrased by James Stephens when he describes Bessie Hannigan in the "Crock of Gold."

> She could listen but not think, she could feel but not know, her eyes looked forward and did not see, her hands groped in the sunlight and found nothing. She listened not with her ears but with her blood. The fingers of her soul stretched out to clasp a stranger's hand, and her disquietude was quickened through with an eagerness which was neither physical nor mental, for neither her body nor her mind was definitely interested. Some dim region between these grew alarmed and watched and waited and did not sleep or grow weary at all.

SUMMARY

The reproductive function presupposes an organism substantially fully developed. Consequently, although the general broad lines of sexual development were established very early in the process, the reproductive organs lie fallow for a long period during which growth of body and adaptation of response are developed before nature returns to the completion of her task.

In contrast with the rapidity of attainment by lower mammals of bodily maturity is the relative tardiness of primate development. Actual bulk is of secondary significance. A relatively long early childhood and rapid adolescence are characteristic of all primates except man, who takes from the sixth to the twentieth birthday to accomplish the development which is covered by the anthropoid in two years. What nature does well she does quickly, but at the cost of considerable strain on the organism. The dangers to life in the adolescent anthropoid are reduced to difficulties or mere disordered progress in the long attenuated adolescence of man.

A long adolescent period maintains a plastic state for accumulation and registration of experience before the human organism crystallizes into maturity.

The human brain is substantially adult in pattern at six years. Thereafter mental development is dominated by finer discriminations of judgment trained by experience. Hence adolescence is characterized by mental, rather than by physical, complexities.

Since adolescence is but a phase of childhood on the threshold of maturity, it falls into the purview of the pediatrician rather than of the internist.

The supposed individual variations in date of inception and in sequence of expression of the phenomena of adolescence are to be attributed to the interplay of factors, mainly internal and endocrine in origin, the combination and precise significance of which are still to be defined.

Intimately bound up with these is the progress to maturity of the skeleton, the adolescent features of which, namely, date and velocity of epiphyseal union, act as a reliable register of progress. On a single examination they give a definition of status. Serial or periodic roentgenographic examination of the skeleton provides a measure of progress.

This physical expression is not an academic finding but an exceedingly important quantitative indicator of constitutional health or defect and may be applied with confidence in the assessment of developmental growth.

THE EFFECT OF VITAMIN B COMPLEX ON THE RESISTANCE OF RATS TO ENTERITIDIS INFECTION *

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As our [1] previous experiments showed that the administration of vitamin D decreased the susceptibility of rachitic rats to an enteritidis infection, it was decided to test the effect of vitamin B, with the same technic. It has been found, as will be shown in the following experiments, that vitamin B in the form of dried yeast [2] increases the resistance of rats on a vitamin B-free diet.

REVIEW OF THE LITERATURE

For many years before it was known that such a substance as vitamin B existed, yeast was used empirically in the treatment for furunculosis and constipation, and recent clinical reports,[3] still justify this practice.

In 1923, Gerstenberger [4] treated a series of patient with herpetic stomatitis and herpes labialis with yeast vitamin tablets (vitamin B concentrate), and found that these conditions, even when they had advanced to the stage of ulceration, were rapidly cleared up by this means. In about one half of the cases Vincent's organisms were present. He believed that the bacterial infection was secondary to a disturbance in metabolism resulting from an insufficient intake of vitamin B. Such a disturbance of metabolism might be described in

* Submitted for publication, June 18, 1931.

* From the Research Laboratories of the Sub-Department of Paediatrics, University of Toronto, and the Hospital for Sick Children, under the direction of Alan Brown, M.D.

1. Robertson, E. C., and Ross, J. R.: Proc. Soc. Exper. Biol. & Med. **27**:999, 1930.

2. The vitamin B complex in dried yeast includes the antineuritic vitamin, variously known as B_1, B or F, the pellagra-preventive vitamin, also known as B_2, or G, and possibly also a third and fourth factor known as B_3, and B_4.

3. Hawk, P. B.; Knowles, F. C.; Rehfuss, M. E., and Clarke, J. A.: Bakers' Yeast, J. A. M. A. **69**:1243 (Oct. 13) 1917. Welker, W. H., and Heintz, E. L.: Arch. Therap. **5**:152 (May) 1926.

4. Gerstenberger, H. J.: Etiology and Treatment of Herpetic (Aphthous and Aphtho-Ulcerative) Stomatitis and Herpes Labialis, Am. J. Dis. Child. **26**:309 (Oct.) 1923.

other words as a state of decreased resistance of the tissues to bacterial injury.

In laboratory experiments, animals lacking vitamin B have been shown to be more susceptible than controls to intraperitoneal injections of various organisms, including pneumococci, meningococci and anthrax bacilli.[5] Werkman and his associates,[6] using rats, also found that about one-half the amount of diphtheria toxin that was lethal for a normal rat would kill an animal deficient in vitamin B. It was also found [7] that if a young rat was deprived of this vitamin, it could be sensitized by the injection of a foreign protein and later killed by anaphylactic shock, whereas similar rats on a normal diet could not be so sensitized. These procedures were all of a highly artificial nature, and in addition the animals were in a state of advanced avitaminosis when the comparative tests were made.

Rowlands [8] put rats on diets partially and completely deficient in vitamin B alternately for twelve weeks. He then fed them 1 cc. of a heavy suspension of streptococci or other organisms. The controls that had received bemax (a source of vitamin B) in addition to the diet were similarly infected. The infection did not cause any apparent disease in the rats, and after four days they were killed. Sections of the intestinal walls of the deficient animals that had been fed streptococci showed these organisms in the lacteals, and they were also present in the intestinal lumen in large numbers. The controls showed only a few streptococci in the lumen and none in the lacteals. The experiments would have been more convincing if an actual infection had been set up.

In one of Rose's [9] experiments on a dog deficient in vitamin B an abscess yielding a pure culture of the Welch bacillus (B. aerogenes-capsulatus) developed at the site of a previous subcutaneous injection of vitamin B solution. The dog recovered rapidly when it was fed large amounts of vitamin B. Dogs on a normal diet could not be infected with this bacillus, but in those on rations deficient in vitamin B positive blood cultures developed which became sterile when the animals were fed vitamin B.

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5. Findlay, G. M.: J. Path. & Bact. **26**:485, 1923.

6. Werkman, C. H.: Immunologic Significance of Vitamin; Influence of Lack of Vitamins and Resistance of Rat, Rabbit and Pigeon to Bacterial Infection, J. Infect. Dis. **32**:255 (April) 1923. Werkman, C. H.; Baldwin, F. M., and Nelson, V. E.: Immunologic Significance of Vitamins; Influence of Lack of Vitamin C on Resistance of the Guinea-Pig to Bacterial Infection on the Production of Specific Agglutinins and on Opsonic Activity, J. Infect. Dis. **35**:549 (Dec.) 1924.

7. Wedgewood, P. E., and Grant, A. H.: Med. Bull., Univ. Cincinnati **2**:172, 1924.

8. Rowlands, M. J.: Proc. Roy. Soc. Med. (Sec. Compar. Med.) **20**:41, 1927; Rep. no. 7, Bemax Lab., February, 1929.

9. Rose, W. B.: Proc. Soc. Exper. Biol. & Med. **25**:657, 1928.

Lassen [10] fed twenty mice deficient in vitamin B and nineteen controls 0.5 cc. of B. aertrycke (Breslau) broth. Some of each group were killed daily to determine if the infection was disseminated more rapidly in the deficiently fed animals. No difference in the rate of spread was revealed. All of the remaining animals died. The mice deficient in vitamin B died on the average in eight days. The controls lived slightly longer, nine and six-tenths days. The difference is probably negligible. The mouse is very susceptible to this infection, and the large dose may have masked any difference in the resistance between the two groups.

Verder [11] fed a B. enteritidis suspension to adult rats on diets deficient in vitamin B and on control diets; she killed them after eighteen and forty-eight hours, and examined the organs bacteriologically. The organism was found in the gastro-intestinal tract, but was not isolated from any of the organs except the spleen of one control animal. Our own experience [12] is that in young rats fed similar diets, the enteritidis organism is found in the spleen and liver forty-eight hours after ingestion.

Ackert [13] and his co-workers have shown that young chickens deprived of vitamin B cannot recover from an artificial infection with ascariasis as well as the controls.

The skin lesions that Cowgill and his associates [14] observed in dogs deficient in vitamin B may have been of infectious origin, although this is doubtful. They cleared up rapidly when vitamin B concentrate was fed. The pellagra-like lesions that Goldberger [15] observed in rats deficient in vitamin B may also have been caused by bacteria, which were, however, provided with a favorable "soil" for growth by the alteration in metabolism caused by the avitaminosis.

Barlow [16] found that spontaneous bacteremia was often present in pigeons fed on a vitamin B-free diet. If sufficient vitamin B was added, the bacteremia was practically inhibited, and if the birds were given an excess of this vitamin, no organisms could be found in the blood. Although the bacteria were not identified, he suspected that they were of intestinal origin.

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10. Lassen, H. C. A.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **63**:110, 1929.

11. Verder, E.: Effect of Diets Deficient in Vitamin A or B on Resistance to Paratyphoid-Enteritidis Organisms, J. Infect. Dis. **42**:589 (June) 1928.

12. Ross, J. R., and Robertson, E. C.: Unpublished data.

13. Ackert, J. E., and Nolf, L. O.: Am. J. Hyg. **13**:337, 1931.

14. Cowgill, G. R.; Stucky, C. J., and Rose, W. B.: Physiology of Vitamins; Cutaneous Manifestations Related to Deficiency of Vitamin B Complex, Arch. Path. **7**:197 (Feb.) 1929.

15. Goldberger, J., and Lillie, R. D.: U. S. Pub. Health Rep. **41**:1025, 1926.

16. Barlow, O. W.: Am. J. Physiol. **93**:161, 1930.

McCarrison [17] found that when wild monkeys were placed on a diet lacking vitamin B, colitis, probably due to Entameba histolytica, developed in about 40 per cent of them. The disease did not develop in controls fed a normal diet, whereas in a third group that lacked vitamin A as well as vitamin B, all were infected.

There is no reduced production of specific agglutinins, bacteriolysins, amboceptor or antitoxin following the injection of appropriate antigens, according to the work of Werkman [18] and Zilva.[19] Blackberg,[20] on the other hand, reported results leading to the opposite conclusion. Werkman [21] showed that the phagocytic index when determined in vivo was slightly depressed in rats lacking vitamin B. When the determination was made in vitro, no difference was evident between the controls and the deficient animals. Findlay and McLean [22] showed that rats lacking vitamin B for twenty-five days or more have a reduced natural bactericidal power for Staphylococcus aureus unassociated with infection. The former author [5] also demonstrated that the peritoneal exudate of pigeons lacking vitamin B has a lowered bactericidal action. However, the capacity of the body to produce antibodies of these types bears no essential relationship to the ability of the body to resist disease.

McCarrison and others have shown that animals lacking vitamin B as well as other vitamins, proteins and inorganic salts, e. g., pigeons fed polished rice, are more susceptible to various infections, but as our experiments are concerned with the lack of vitamin B only, these reports are not applicable to the question under discussion.

EXPERIMENTS

Material.—Four weeks old albino rats were used. The breeding rats were fed a standard well balanced diet. The litters were kept apart, divided in two, and the larger rats (from 2 to 3 Gm. heavier) were put in the group that was to be given the diet deficient in vitamin B. The smaller rats were given the same diet supplemented with yeast. After the rats had been on the diet from one to eight days, about half of each group were infected, and the rest were kept as diet controls. When they were infected, the rats fed the diet deficient in vitamin B plus yeast were on the average 2 Gm. heavier (45 Gm.) than the rats on the diet deficient in vitamin B (43 Gm.).

17. McCarrison, R.: Proc. Roy. Soc. Med. **18**:3, 1925.

18. Werkman, C. H.: (Footnote 6); Immunologic Significance of Vitamins; Influence of Lack of Vitamins on Production of Specific Agglutinins, Precipitins, Hemolysins and Bacteriolysins in Rat, Rabbit and Pigeon, J. Infect. Dis. **32**:247 (April) 1923.

19. Zilva, S. S.: Biochem. J. **13**:172, 1919.

20. Blackberg, S. N.: Proc. Soc. Exper. Biol. & Med. **25**:770, 1928.

21. Werkman, C. H.: Immunologic Significance of Vitamins; Influence of Lack of Vitamins on Leukocytes and on Phagocytosis, J. Infect. Dis. **32**:263 (April) 1923.

22. Findlay, G. M., and McLean, I.: Biochem. J. **19**:63, 1925.

The diet deficient in vitamin B [23] consisted of: Vitamin B-free casein, 18 per cent; dextrin, 71.3 per cent; agar agar, 2 per cent; butter fat, 5 per cent; cod liver oil, 2 per cent, and salt mixture (McCollum's no. 185), 3.7 per cent. The controls were fed the same diet with the addition of 6 per cent of powdered dried brewer's yeast (Mead Johnson & Company).

The rats were kept in cages with wire-meshed bottoms to prevent coprophagy if possible. After they were infected, one or at most two animals were put in a cage with a floor area of 14½ by 9 inches (36 by 23 cm.) made of ⅜ inch (1.15 cm.) wire mesh.

The Infecting Organism.—A Salmonella strain, known as S. muriotitis, which was originally isolated from the infected middle ear of an albino rat by McCor-

TABLE 1.—*Rats Fed Original Culture of S. Muriotitis*

Experiment	Amount of Culture Fed, Cc.	Rats on Diet Deficient in Vitamin B		Rats on Diet Deficient in Vitamin B Plus 6% Yeast	
		Deaths	Survivors	Deaths	Survivors
1	0.03	5	0	1	5
2	0.05	4	2	0	5
3	2.00	5	0	0	6
4	2.00	5	0	0	5
Total number.....		19	2	1	21
Total per cent.....		90	10	5	95

TABLE 2.—*Rats Fed New Culture of S. Muriotitis*

Experiment	Amount of Culture Fed, Cc.	Rats on Diet Deficient in Vitamin B		Rats on Diet Deficient in Vitamin B Plus 6% Yeast	
		Deaths	Survivors	Deaths	Survivors
5	0.5	5	0	3	1
6	0.2	4	2	2	5
7	0.15	3	0	2	1
8	0.1	5	0	3	2
9	0.05	7	6	2	8
Total number.....		24	8	12	17
Total per cent.....		75	25	41	59

dock,[24] in 1925, was used as the infecting agent. A small amount of an eighteen hour broth culture (tables 1 and 2) grown at 37 C. was fed to each rat on a small cube of dried bread after the animal had been starved for about twenty hours. The bread absorbed the broth readily so that none was lost, and the rats were put singly in cages with solid bottoms for the feeding to make sure that all of the crumbs were eaten. When the bread was completely eaten, the former diet was restored.

This strain (S. muriotitis) has the same biologic reactions as S. enteritidis, although according to McCordock it is serologically distinct. S. enteritidis is known to be the cause of severe and often fatal diarrhea among rats.[25] Pre-

23. McCollum, E. V., and Simmonds, N.: J. Biol. Chem. **33**:55, 1918.

24. McCordock, H. A.: Bull. Johns Hopkins Hosp. **37**:412, 1925.

25. Meyer, K. F.: Newer Knowledge of Bacteriology and Immunology, Chicago, University of Chicago Press, 1928, p. 637.

vious to artificial infection, blood and fecal cultures were made in another series of fifty and eighty-four rats, which, however, were on a rachitic diet, and the organism was recovered from 4 and 3.5 per cent of the animals, respectively. The infection was therefore not common naturally in our rats, and also only one death from any cause occurred among the uninfected animals on control diets in the following experiments.

Postmortem Examinations.—The rats were examined as soon as possible after death, and cultures were taken from the heart under sterile precautions. If the organism recovered was lactose-negative and was agglutinated in dilutions of 1:1,000 or over by a specific immune rabbit serum, it was considered to be S. muriotitis. In eight instances, the rats had been dead too long for bacteriologic examination, and these deaths were taken as due to the S. muriotitis infection.

The survivors were killed and examined twenty-eight days or more after they were infected. Cultures from the heart's blood were sterile in all, and only two cultures from the liver yielded S. muriotitis, which would mean that these rats had been infected but had not been able to get rid of all the organisms.

None of the thirty-nine uninfected controls deficient in vitamin B died before the experiments were terminated, which is fairly conclusive evidence that the deaths after the infection were not due to the deficiency of vitamin B. Of the thirty-eight uninfected controls on the diet supplemented with yeast, one died from an undetermined cause. The rats fed the diet supplemented with yeast gained rapidly in weight in contrast to those on the diet deficient in vitamin B, which, after gaining at a moderate rate for about two weeks, began to lose, with the result that they weighed about as much at the end as they did at the beginning of the experiment. Of the rats that were fed the diet supplemented with yeast, those that were infected did not gain as much in the twenty-eight days of the experiment as the other rats on the same diet (the so-called diet controls) which were not infected. The average gain in weight of the infected rats on the diet supplemented with yeast was 43.3 Gm., whereas the average gain in weight of the noninfected controls given the same supplemented diet was 70.6 Gm.

The probable explanation of this lower rate of growth of the infected animals is that it is due to the presence of the infection. It confirms us in the opinion that the enteritidis organism caused disease in the yeast-fed rats from which they were able to recover. Price-Jones[26] reported a similar result in rats infected per os with B. enteritidis as compared with normal noninfected animals.

RESULTS

The results of the first four experiments are shown in Table 1. It is quite evident that the rats that received yeast as a supplement to the diet withstood the infection much better than those on the diet deficient in vitamin B. The virulence of the infecting culture decreased markedly after the second experiment, and the dose had to be increased forty times in the next two experiments. A new culture was then obtained from the original source (American Type Culture Collection), and this seemed to be about as virulent as the first culture was originally. This was used in the five experiments shown in table 2 in decreasing doses. The doses in experiments 5, 6, 7 and 8 were too large, and the results are

26. Price-Jones, C.: J. Path. & Bact. **30**:45, 1927.

less striking, although in every case the rats fed the yeast survived in larger numbers. The dose in experiment 9 was a little too small, but the rats deficient in vitamin B again did not withstand the infection as well.

COMMENT

As the rats placed on the diet deficient in vitamin B were infected within from one to eight days after the diet was begun, and as the experiments were terminated four weeks after infection, it is probable that a deficiency in vitamin B_2, or G, played a very minor part, and that a deficiency of the B_1 factor was responsible for the decreased resistance to infection. Rats on a diet deficient in vitamin B show signs of the deficiency in about two weeks, and some of them begin to die of the avitaminosis after about five weeks, whereas it takes approximately four weeks for rats deficient in vitamin B_2 to show evidence of the deficiency.

It is also possible, although not likely, that the beneficial effect of the yeast is not due to its high vitamin B content. The addition of 3 per cent more protein (dried yeast is about half protein) would not alter the diet to any appreciable extent, but yeast is also a very rich source of purine bases,[27] and it also contains bios as well as a substance that prevents pink disease in rats.[28] The effect of the last three factors on resistance to disease has as yet not been determined, so far as we are aware.

DETAILS OF EXPERIMENTS

In experiment 1 (table 1) the rats were given the diet seven days before infection and the five animals on the diet deficient in vitamin B died in three, seven, fourteen, fifteen and twenty days, respectively. The rat fed yeast in addition to the diet died in ten days.

In experiment 2 the rats were given the diet seven days before infection, and the four animals on the diet deficient in vitamin B died in fourteen, fourteen, fourteen and twenty-five days.

In experiment 3 the rats were given the diet eight days before infection, and the five animals on the diet deficient in vitamin B died in twelve, twelve, eighteen, twenty and twenty-four days.

In experiment 4 the rats were given the diet one day before the infection, and the five animals on the diet deficient in vitamin B died in eight, eleven, sixteen, seventeen and twenty-three days.

In experiment 5 (table 2) the rats were given the diet four days before infection. The five animals on the diet deficient in vitamin B died in two, three, nine, nine and eleven days. The three rats fed yeast in addition to the diet died in four, five and sixteen days.

In experiment 6 the rats were given the diet one day before infection and the four animals on the diet deficient in vitamin B died in eleven, twelve, eighteen and twenty-one days. The two rats fed yeast in addition to the diet died in eleven and sixteen days.

27. Osborne, T. B.: New York State J. Med. **20**:217, 1920.
28. Megaw, J. W.: Proc. Roy. Soc. Med. **23**:733, 1930.

In experiment 7 the rats were given the diet one day before infection, and the three animals on the diet deficient in vitamin B died in ten, eleven and eighteen days. The two rats fed yeast in addition to the diet died in thirteen and seventeen days.

In experiment 8 the rats were given the diet one day before infection, and the five animals on the diet deficient in vitamin B died in twelve, thirteen, fifteen, seventeen and eighteen days. The rats fed yeast in addition to the diet died in twelve, fourteen and fifteen days.

In experiment 9 the rats were given the diet one day before infection, and the seven animals on the diet deficient in vitamin B died in eleven, sixteen, eighteen, twenty-one, twenty-eight, twenty-eight and twenty-eight days. The two rats fed yeast in addition to the diet died in twelve and fourteen days.

SUMMARY

1. A group of young rats were fed a vitamin B-free diet, and a second group were fed a similar diet plus 6 per cent dried brewers' yeast. Both groups were infected per os with an enteritidis organism. Of fifty-three rats deficient in vitamin B ten, or 19 per cent, survived the infection, whereas of the fifty-one rats given the yeast in addition, thirty-eight rats, or 75 per cent, survived the infection (See table 3).

2. The addition of the vitamin B complex to a diet lacking in this factor increased the resistance of rats against infection.

TABLE 3.—*Summary of Tables 1 and 2*

Experiments	Rats on Diet Deficient in Vitamin B		Rats on Diet Deficient in Vitamin B Plus 6% Yeast	
	Percentage of Deaths	Percentage of Survivors	Percentage of Deaths	Percentage of Survivors
1 to 4	90	10	5	95
5 to 9	75	25	41	59
Total percentage of tables 1 and 2	81	19	25	75

SOME FACTORS INFLUENCING THE FECAL FLORA OF INFANTS*

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For a number of years one of us (G.[1]) has been studying the chemical composition of the stools of infants with special reference to the influence of various diets, particularly the carbohydrates. The infants under observation were kept in a special nursery under the supervision of a special nurse, provided by the hospital administration and training school, thus minimizing the possibility of accidental intercurrent infections. They entered the hospital at the age of from 2 to 3 weeks and remained until about 6 months of age. The carefully controlled factors presented an unusual opportunity for extensive study of the bacteriology of the stools of these infants as well as an attempt to correlate the types of fecal bacteria with the chemical composition of the stool.

REVIEW OF THE LITERATURE

Significance of Gastro-Intestinal Bacteria.—From 1719, when Antony von Leeuwenhoek used his newly devised microscope to discover mysterious particles in the intestinal excretions, to 1886, when Escherich[2] wrote his great monograph, the subject of gastro-intestinal bacteriology had hardly been opened. The development of the microscope led early writers to speculate as to the significance of gastro-intestinal bacteria. As far back as 1846, Frerich[3] wrote, "The bacteria neither aid nor interfere with digestive processes." In 1881, some years before

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1. Gerstley, J. R.: Influence of Feeding on Certain Acids in Feces of Infants, Am. J. Dis. Child. **40**:27 (July) 1930. This article contains the bibliography of previous work done with Wang et al.

2. Escherich, T.: Die Darm Bacterien des Säuglings, Stuttgart, Ferdinand Enke, 1886.

3. Frerich, in Wagner, R.: Handwörterbuch der Physiologie, Braunschweig, F. Vieweg u. Sohn, 1846, vol. 3, p. 869.

Escherich's observations, Uffelmann [4] began to study some of the characteristics of the organisms found in the feces. Pasteur [5] believed that these organisms were absolutely necessary to life, and attempted experiments to test his theory. Frerich, on the other hand, believed the intestinal flora unessential and merely the result of residues of diet and gastro-intestinal processes with no particular function. The tendency of later investigators, for example Bessau,[6] Davison and Rosenthal,[7] Mitchell,[8] Kendall [9] and others, is to confirm the early theory of Frerich. Kendall sums up the subject by stating that the intestinal bacteria are the result of the influence of nutritional stimuli plus the ability of the organisms to grow in the intestinal environment. However, the acid-producing flora may be a factor in restricting the growth of other bacteria.

Bacterial Types in the Breast-Fed.—Although Escherich in 1886 made the first authoritative study of gastro-intestinal flora of infants, it remained for Henri Tissier [10] to show that in the feces of the breast-fed infants there were relatively few colon bacilli and a predominance of bacteria that he called B. bifidus. Some years later Finkelstein,[11] and again Moro,[12] in isolating B. acidophilus showed that the gram-positive organisms were not a single type but a group. Mereshkowsky,[13] Kendall and Haner,[14] Stransky and Wasitsky [15] and many others have studied the characteristics of the individual members of this group.

Implantation.—As the uniformly gram-positive bifidus-acidophilus group seems to typify ideal nutritional conditions in the infant, early investigators suggested that the gram-negative flora found in artificially fed infants might have been due to the introduction of extraneous

4. Uffelmann, J.: Deutsches Arch. f. klin. Med. **28**:437, 1881.

5. Pasteur, L.: Gaz. hebd. de méd., 1885, vol. 32.

6. Bessau, G.: Jahrb. f. Kinderh. **92**:4, 1920; Klin. Wchnschr. **2**:861, 1923.

7. Davison, W. C., and Rosenthal, L. V.: A Bacteriological Study of Fecal Flora of Infants and Children (Lack of Association of Nutritional Disorders with a So-Called "Putrefactive" Intestinal Flora), Am. J. Dis. Child. **22**:284 (Sept.) 1921.

8. Mitchell, H. S.: Am. J. Physiol. **79**:537 and 542, 1927.

9. Kendall, A. I.: Bacteriology, General, Pathological and Intestinal, Philadelphia, Lea & Febiger, 1928, chap. 29, p. 661.

10. Tissier, H.: Flore intestinale des nourrissons, Paris, 1900; Ann. Inst. Pasteur **19**:109, 1905; Compt. rend. Soc. de biol. **51**:943, 1899.

11. Finkelstein, H.: Deutsche med. Wchnschr. **22**:362, 1900.

12. Moro, E.: Jahrb. f. Kinderh. **52**:38, 1900.

13. Mereshkowsky, S. S.: Centralbl. f. Bakt. **39**:380, 584 and 696, 1905; **40**:118, 1905.

14. Kendall, A. I., and Haner, R. C.: Bacillus Bifidus, J. Infect. Dis. **35**:77,; 1923; Bacillus Acidophilus, ibid. **35**:89, 1923.

15. Stransky, E., and Wasitsky, A.: Monatschr. f. Kinderh. **47**:517, 1930.

organisms. In 1907, Belanowsky,[16] and before him, in 1898, de Jaeger,[17] showed that sterilizing mixtures of cow's milk did not prevent characteristic gram-negative fecal flora from growing. Since the time of Metchnikoff, Brudzinzki,[18] Mereshkowsky,[13] Dunn,[19] Rettger,[20] Paulson [21] and many others have attempted the implantation of gram-positive organisms in adults and in animals. Brown and Bosworth [22] have offered the most convincing evidence that B. bifidus flora is an implantation from organisms present on the nipples.

Factors Involved in the Maintenance of a Gram-Positive Flora.—The pediatrician is especially interested in the factors involved in the maintenance of the bifidus-acidophilus flora. This problem has been studied by Rodella,[23] Moro,[24] McNease and Cannon,[25] Sengenhoff,[26] and Tissier and Dreyfus.[27] They agree that the chemical composition of breast milk is responsible for the predominance of the gram-positive flora. Jacobson [28] was able to produce this flora by feeding breast milk to dogs.

The factor in breast milk responsible for the flora has been subjected to intensive research. As early as 1857, clinical observation pointed to the importance of carbohydrate in overcoming intestinal putrefaction. At that time, Behrens, Siebers and Moore [29] noted that the putrefactive stools of a 16 months old child were corrected by one teaspoonful of sugar every hour. Escherich, in 1886, suggested the importance of lactose, as did Sittler [30] twenty-two years later. Gregor [31] noted that in infants fed on Keller's malt soup (50 Gm. of wheat flour is

16. Belanowsky, G.: Centralbl. f. Bakt. **44**:322, 1907.

17. de Jaeger, quoted by Brudzinski: Jahrb. f. Kinderh. **52**:469, 1900.

18. Brudzinzki: Jahrb. f. Kinderh. **52**:469, 1900.

19. Dunn, C.: Arch. Pediat. **24**:241, 1907.

20. Rettger, L. F.: Am. J. Pub. Health **19**:771 (July) 1929.

21. Paulson, M.: Bull. Johns Hopkins Hosp. **45**:315, 1929.

22. Brown, E. W., and Bosworth, A. W.: Studies in Infant Feeding; Bacteriologic Study of Feces and Food of Normal Babies Receiving Breast Milk, Am. J. Dis. Child. **23**:243 (March) 1922.

23. Rodella, I.: Centralbl. f. Bakt. **29**:718, 1901.

24. Moro, E.: Jahrb. f. Kinderh. **11**:687, 870, 1905.

25. McNease, B. W., and Cannon, P. R.: Factors Controlling Intestinal Bacteria, Influence of Hydrogen-Ion Concentration in Bacterial Types, J. Infect. Dis. **32**:175 (March) 1923.

26. Sengenhoff, A.: Monatschr. f. Kinderh. **40**:263, 1928.

27. Tissier, H., and Dreyfus, S.: Compt. rend. Soc. de biol. **92**:476, 1925.

28. Jacobson: Comp. rend. Soc. de Biol. **67**:143, 1909.

29. Behrens, Siebers and Moore, quoted by Escherich (footnote 2).

30. Sittler, P.: Centralbl. f. Backt. **47**:14 and 145, 1908; Monatschr. f. Kinderh. **1**:763, 1908.

31. Gregor: Arch. f. Kinderh. **29**:595, 1900.

warmed in 0.33 liter of cow's milk; 100 Gm. of Loefland's malt soup extract—malt extract neutralized with potassium carbonate—is dissolved in 0.67 liter of water, and these mixtures are combined and heated to 100 C.) gram-positive flora tended to develop. Moro [32] thought the dominant factor was not in the carbohydrate alone, but in the whey of breast milk. Finkelstein and Meyer,[33] in 1910, emphasized the importance of casein, Bahrt and Beifeld [34] in the same year stressed the significance of calcium and its relation to carbohydrate in the food, while in 1924, Ruhle [35] reverted to casein. In 1917 and 1921, Hull and Rettger [36] and Rettger and Cheplin [37] wrote extensively on the importance of an excess of lactose in the diet. These results were commented on pro and con by Torrey,[38] Cannon,[39] Sisson [40] and Bass.[41] Only recently, Barenberg and Abramson [42] were not entirely convinced as to the exact rôle of lactose. During this controversy, few have paid attention to the studies of Kendall,[9] who, in 1910, in experiments on cats, dogs and monkeys, showed the importance of the relation of lactose to protein in maintaining a gram-positive flora.

The problem has been studied from a strictly bacteriologic standpoint by Adam [43] and Adam and Froboese.[44] Adam's later work investigated the factors affecting the growth of B. bifidus in the test tube. Dextrose, saccharose and lactose, as well as acid casein, alkali soap and iron, accelerated the growth of B. bifidus, while dextrin, starch, amino-acids, albumin and calcium soaps and salts inhibited growth. Adam concluded that breast milk in the intestine led to the presence of all the accelerating factors. On the other hand, Schoenfeld [45] was unable to confirm much of the previous work, and believed that there is a specific factor in breast milk, independent of any of the known chemical constituents. His work received some corroboration in the recent publi-

32. Moro, E.: Monatschr. f. Kinderh. **6**:550, 1907-1908; Arch. f. Kinderh. **43**: 340, 378 and 427, 1906.

33. Finkelstein, H., and Meyer, L. F.: Jahrb. f. Kinderh. **21**:525, 1910.

34. Bahrt, H., and Beifeld, A.: Jahrb. f. Kinderh. **60**:187, 1926.

35. Ruhle, R.: Jahrb. f. Kinderh. **104**:39, 1924.

36. Hull, T. H., and Rettger, L. F.: J. Bact. **2**:47, 1917.

37. Rettger L. F., and Cheplin, H. A.: Transformation of the Intestinal Flora, New Haven, Conn., Yale University Press, 1921.

38. Torrey: J. M. Research **39**:15, 1919.

39. Cannon, P.: J. Infect. Dis. **29**:369 (Oct.) 1921.

40. Sisson, W. R.: Intestinal Flora, Am. J. Dis. Child. **13**:117 (Feb.) 1917.

41. Bass, C. C.: South. M. J. **16**:1, 1923.

42. Barenberg, L. H., and Abramson, H.: Arch. Pediat. **47**:1, 1930.

43. Adam, A.: Ztschr. f. Kinderh. **31**:331, 1922; Jahrb. f. Kinderh. **60**:187, 1926.

44. Adam, A., and Froboese: Ztschr. f. Kinderh. **39**:267, 1925.

45. Schoenfeld, H.: Jahrb. f. Kinderh. **63**:19, 1926.

cation of Rosenthal and Lieberman.[46] They believe that they isolated a substance in breast milk, "lysozyme," that is not present in cow's milk which encourages the growth of B. bifidus by its inhibiting effect on the colon bacillus.

The introduction of lactic acid milk to the dietary used in our experiments has opened the question as to the effect of the addition of lactic acid to cow's milk. Margaret Upton[47] investigated this in the use of three types of feedings: (1) milk soured bacterially, probably by Streptococcus lacticus; (2) sterile whole cow's milk, and (3) evaporated milk diluted with equal parts of sterile water plus 0.5 per cent lactic acid and 9 per cent dextrose corn syrup.

She noted little difference in the intestinal flora after any of these feedings, and it never resembled that of the breast-fed infant. She noted also that the flora of the bottle-fed infant varied day by day, and that in the breast-fed infant, a parenteral infection led to a diminution of the gram-positive flora with an increase of B. coli.

EXPERIMENTAL PROCEDURE

The babies studied were normal infants over 2 weeks of age, kept in a separate nursery. The artificial feedings consisted of the following: (1) whole cow's milk boiled one minute; (2) whole cow's milk plus 3 per cent lactose; (3) whole cow's milk plus 12 per cent lactose; (4) whole lactic acid milk made by the addition of 1.5 drachms (90 drops or 5.8 Gm.) of lactic acid to 1 quart of whole cow's milk; 3 per cent and later 12 per cent lactose was also added to the lactic acid milk, and (5) fermented lactic acid milk (two babies).

The six normal infants selected for the bacteriologic observations were fed breast milk for at least two weeks. Smears and bacterial cultures of the feces of each infant were made (daily for four infants and at two-day intervals for two infants), both when the infant was under the customary nursery regimen and when the infant was on the metabolism bed. The diet of the infants was changed every three weeks by the addition of lactose to the breast milk or by the substitution of one of the artificial feedings mentioned in the foregoing paragraph. With every change of diet, the bacterial flora of the feces was studied to determine whether the gram-positive flora with B. bifidus predominating, so characteristic of the stools of infants fed with breast milk, was maintained, or whether the gram-negative flora with B. coli predominating, which is typical of the feces of the infant fed with cow's milk, resulted.

Although the bacteriologic composition of the stool was thus considered chiefly from the standpoint of gram-negative or gram-positive flora, group classification was made almost as a routine measure. When it was possible to identify individual strains by morphology or routine cultural methods, such identification was made. However, immunologic methods, such as agglutination with various antiserums or

46. Rosenthal, L., and Lieberman, Hyman: Rôle of Lysozyme in Development of Intestinal Flora of New-Born Infant, J. Infect. Dis. **48**:226 (Feb.) 1931.

47. Upton, M.: Anaerobic Intestinal Flora of Normal Breast-Fed and Artificially Fed Infants, Am. J. Dis. Child. **37**:1221 (June) 1929.

agglutinin-absorption tests, were not employed to disinguish closely allied strains such as those of the aciduric group.

There was some diversity in the sequence in which the various feedings were given to the infants so that the influence of age on the fecal flora might be noted. The order of the different feedings of the infants was as follows:

Infant 1: Breast milk, fermented whole lactic acid milk, fermented whole lactic acid milk with 3 per cent lactose, fermented whole lactic acid milk with 12 per cent lactose and whole cow's milk with 12 per cent lactose.

Infant 2: Breast milk, whole cow's milk, whole lactic acid milk and whole lactic acid milk with 3 per cent lactose.

Infant 3: Breast milk, whole lactic acid milk, whole cow's milk, boiled milk (breast milk), whole cow's milk with 3 per cent lactose, whole cow's milk with 12 per cent lactose, whole cow's milk and whole lactic acid milk.

Infant 4: Cow's milk with 3 per cent lactose, breast milk, breast milk with 12 per cent lactose, whole cow's milk, whole cow's milk with 3 per cent lactose, whole cow's milk with 12 per cent lactose, whole cow's milk and whole lactic acid milk.

Infant 5: Breast milk, breast milk with 12 per cent lactose, whole cow's milk (reduced quantities), whole cow's milk (increased quantities), whole cow's milk with 3 per cent lactose, whole cow's milk with 12 per cent lactose, whole cow's milk, whole lactic acid milk, whole lactic acid milk with 3 per cent lactose and whole lactic acid milk with 12 per cent lactose.

Infant 6: Breast milk, breast milk with 12 per cent lactose, whole lactic acid milk, fermented lactic acid milk, whole lactic acid milk with 3 per cent lactose, whole lactic acid milk with 12 per cent lactose, whole lactic acid milk with 12 per cent dextrimaltose, whole lactic acid milk with 12 per cent lactose, whole lactic acid milk, whole cow's milk and whole cow's milk with 3 per cent lactose.

TECHNIC

1. A sample of the feces was obtained by inserting a sterile glass tube (3 mm. in diameter) about 1 inch into the rectum of the infant. The tube containing the material was then kept in a sterile test tube.

2. A direct smear of the feces was made on a slide and stained by Gram's method. In this way the predominance of gram-positive or gram-negative organisms was determined. Counts of the varieties of bacteria and their proportionate numbers were attempted, but proved unsatisfactory. Therefore, we differentiated the flora as gram-negative (over 70 per cent), gram-positive (over 90 per cent) or mixed (in about equal proportion).

3. Anaerobic cultures were made primarily for the detection of B. bifidus. A loopful of the material was streaked on a blood agar plate and incubated for four days in an anaerobic culture apparatus (McIntosh and Fildes, improved model).

4. The feces were cultivated aerobically on blood agar plates, on which most of the organisms seen in smears could be isolated. Endo-agar was used for the rapid detection of bacteria belonging to the colon-aerogenes group. A large loopful of the material was inoculated into a test tube of dextrose veal broth to assure the growth of streptococci. For the culture of bacteria belonging to the bifidus-acidophilus group, a 0.25 per cent acetic acid broth (Kendall) was tried. This was supplanted by a 10 per cent ascites broth which was slightly acid. Contrary to the accepted fact that B. bifidus is considered an obligatory anaerobe and B. acidophilus an aerobe or a facultative anaerobe, both the organism, morphologically

B. bifidus, from the breast-fed infant and the organism, morphologically B. acidophilus, from the infant fed on cow's milk with 12 per cent lactose grew in this medium. A tube of saccharose was inoculated to determine acid and gas-producing bacteria in the feces. Acid was detected on all occasions and gas at frequent intervals.

BACTERIOLOGY RESULTING FROM THE VARIOUS DIETS

The direct gram-stained smears from the breast-fed infant showed a predominance of gram-positive organisms of the B. bifidus type, with relatively few B. coli and M. ovalis. The addition of 12 per cent lactose to the breast milk did not change this flora, except for an occasional B. bulgaricus. When the feedings were changed from breast milk to artificial feedings of either whole cow's milk or whole lactic acid milk, there was always an abrupt change within twenty-four hours from the gram-positive flora to a mixed bacterial flora.

There was no marked difference between the bacterial flora when the infant was fed whole cow's milk and when it was fed whole lactic acid milk. B. coli was the predominating organism, and the numbers of the following organisms varied from day to day: Streptococcus anhemolyticus, B. bulgaricus, B. proteus, B. alkaligenes, diphtheroids and B. mucosus. With the addition of 3 per cent lactose to whole cow's milk, the bacterial flora remained mixed. However, 12 per cent lactose added to whole cow's milk changed the flora within two weeks from gram-negative organisms to a predominance of gram-positive bacteria of the bifidus-acidophilus type. The direct smears were similar to those of the breast-fed infant.

The mixed bacterial flora of the infant on whole lactic acid milk was not changed by the addition of 3 per cent lactose, but the addition of 12 per cent lactose within a week changed the flora to gram-positive. For two babies, fermented lactic acid milk was used, and lactose added in 3 per cent and 12 per cent quantities. The direct smears were similar to those of the infants on whole lactic acid milk diets. Infant 3 was fed whole lactic acid milk for a period of two months, and the bacterial flora of the stools during that time was mixed, consisting of B. coli, B. bulgaricus, B. mucosus, streptococcus, B. saccharobutyricus and a few B. acidophili. After a month's time, the flora of the stools remained mixed, but there were more gram-positive bacilli of the bifidus-acidophilus type. At the end of the two months, the direct smears showed B. coli, B. bulgaricus, streptococcus, B. mucosus, B. acidophilus and occasionally B, saccharobutyricus. There were apparently more B. acidophili, but never in predominance.

The bacterial flora of the feces of the six infants studied seemed to be fairly well established with each of the different feedings. Infant 3, however, although given breast milk feedings, had an unstable fecal flora. There was fluctuation between gram-positive and mixed bacteria. There

were several factors that may have caused this variation in flora; for example, the child had an elevation in temperature during this period, the wet-nurse was ill for several days, and the number of feedings per day varied. It was suspected that the breast milk might have been diluted with cow's milk, but investigation indicated otherwise, and the chemical determination confirmed a breast milk diet. The variation and sequence in which the infant received the diets did not make any difference in the bacterial flora obtained from the stools.

Cultures of the breast milk and artificial feedings at various times showed the following organisms: B. bulgaricus, Streptococcus lacticus, B. mucosus and staphylococcus. A parallel study of the feces did not result in a predominance of the organisms isolated from the feedings. Even feedings of fermented lactic acid milk containing large numbers of Streptococcus lactici did not cause an overwhelming number of these organisms in the stool. It seemed, therefore, that there was little or no apparent correlation between the organisms found in the feedings and those isolated from the feces.

During the period of observation the infants were placed on the metabolism bed [1] at frequent intervals for twenty-four hours at a time. Bacteriologic examinations, smears and cultures were made before the infant was placed on the metabolism bed, after five hours and just as the baby was removed from the bed (twenty-four hours). No appreciable change in flora was noted at these times or on succeeding days; for example, infant 1, while on the feeding of breast milk, showed the typical intestinal flora of B. bifidus as the predominating organism, and a few B. coli and M. ovalis. The smears and cultures after the infants had been on the metabolism bed for five hours were identical. The twenty-four, forty-eight and seventy-two hour specimens still revealed B. bifidus, M. ovalis and B. coli. The same observation was made when the infants were on a diet of artificial feedings, whether the diet consisted of whole cow's milk or whole cow's milk with the additional factor. One example will demonstrate: An infant fed fermented lactic acid milk revealed a mixed bacterial flora in the feces, consisting of B. coli, B. bulgaricus, streptococcus and M. ovalis. The five hour and twenty-four hour specimens contained the identical organisms in apparently the same proportion.

Chemical determinations [48] were made on the stools that were obtained during the period when the infants were on the metabolism bed. When the infants were given feedings of breast milk, the stools were usually soft, smooth in consistency, yellow or green and had a characteristic odor. When the feedings consisted of whole cow's milk, lactic acid

48. These determinations were made in the Chemistry Department of Nelson Morris Institute under the direction of Dr. David J. Cohn.

milk, either plain or with the addition of 3 per cent lactose, the stools were often darker, formed and had a putrefactive odor. The feces of the infants fed on varying diets differed in their acidity, as shown by hydrogen ion determinations and determinations of total titrable acidity. The stools of the infants receiving cow's milk, cow's milk plus 3 per cent lactose, whole lactic acid milk with or without 3 per cent lactose or fermented lactic acid milk were more alkaline than those of children fed breast milk or cow's milk plus 12 per cent lactose. This does not mean that all the stools of infants given the first group of feedings were definitely alkaline, or that all those of the second group were definitely acid. In general, the range of p_H for the first group was from 6 to 8, that of the second group from 3 to 7. Concurrent with these differences of p_H, there was a general tendency for the flora of the more alkaline stools to be mixed or with gram-negative organisms predominating, and for those of the acid stools to be predominantly gram-positive. In brief, the addition of 12 per cent lactose to boiled whole cow's milk or lactic acid milk resulted in a stool similar to that obtained from a breast-fed infant.

In several cases parallel studies were made on the nasopharyngeal flora and the intestinal flora of the infants under observation. Smears and cultures of the nasopharynx revealed in varying proportion Staphylococcus albus, anhemolytic streptococcus and diphtheroids. Although a few of these bacteria could be detected in the feces, none was at any time the predominating organism.

Otitis media developed in one of the infants during the course of our study. The diet at that time was whole lactic acid milk plus 3 per cent lactose. The bacterial flora of the feces of this infant corresponded with that of the normal infant on the same feedings, except that there were a few more staphylococci.

COMMENT

Our studies indicate that the bacteria of the infant's feces is dependent on the type of feeding and is not greatly influenced by bacteria introduced extraneously into the food or from the nasopharynx. Indeed, the fecal flora not only depends on the diet, but is a delicate index of the composition of the diet used. A change from breast milk to cow's milk transforms the fecal flora immediately. To reverse the results of the experiment, however, takes longer. Our experiments confirm the observations of Brown and Bosworth and those of Upton in showing how long the influence of cow's milk or lactic acid milk is exerted in the intestine. It takes about two weeks after feedings of the latter type have been discontinued and breast milk given exclusively for the intestinal environment to return again to a state favoring the gram-positive flora. An excellent illustration of the sensitiveness of the flora to change of food was obtained when a mistake in formula substituted a maltose dextrin preparation for lactose. The prompt appearance of a gram-

negative flora in smear and culture was sufficiently striking to institute an immediate investigation, which led to the detection of the error. Studies along these lines will be reported in subsequent publications.

Our studies are strikingly in accord with those of Upton in that we found the flora of infants given feedings of whole lactic acid milk to be identical with those of infants given whole cow's milk. At first we wondered if the addition of lactic acid to cow's milk, by facilitating protein digestion and absorption, would lead to an ideal condition, such as prevailed in breast milk feedings, and lead to a gram-positive fecal flora. This is not the case. No matter what the effect of the addition of lactic acid to cow's milk on gastric digestion, the fecal flora of infants on such feedings is entirely different from that when breast milk is given. The gram-positive fecal flora depends on other factors, namely, definite relation of carbohydrate to protein. Possibly the addition of lactic acid may have had some influence in one experiment. When 12 per cent lactose was added to lactic acid milk, the flora became gram-positive some days sooner than when 12 per cent lactose was added to cow's milk.

The importance of the relation of lactose to protein offers interesting confirmation of the work done years ago by Kendall [9] on animals as well as corroboration of our own chemical and clinical studies.[1] Three per cent lactose caused very little chemical change, and it did not seem to affect the fecal flora in any way. However, when the lactose was increased to 12 per cent in either whole cow's milk or lactic acid milk, and the relation between lactose and protein established similar to that in breast milk, in spite of the obvious overfeeding of the infant and the unquestionable unsuitability of the diet to the child's ultimate health, the feces in respect to hydrogen ion concentration, lactic acid, titrable acidity, color, odor and consistency took on the characteristics of those of the breast-fed infant. In a similar manner, the increase of lactose to 12 per cent in both cow's milk and lactic acid milk resulted in changes in the flora characteristic of the breast-fed infant, and developed in about two weeks when proper relations of acidity had been established in the intestines. Certainly, the relation of lactose to protein is of great importance in determining the characteristics of the feces of the breast-fed infants.

SUMMARY AND CONCLUSIONS

A bacteriologic study was made of the feces of six infants while they were given breast milk feedings and later when they were given various artificial feedings.

The cultures of the feces from the infants fed breast milk resulted in the "normal flora," consisting of B. bifidus and a few M. ovalis and B. coli.

A diet of whole cow's milk, whole lactic acid milk or fermented lactic acid milk resulted in an apparently identical mixed or gram-negative bacterial flora.

The addition of 3 per cent lactose to whole cow's milk or whole lactic acid milk caused little change in the fecal flora unless the diet was continued over a long period (infant 3).

The addition of 12 per cent lactose to whole cow's milk or to whole lactic acid milk resulted in a gram-positive flora similar to that obtained from the stools of breast-fed infants.

The sequence in which the feedings were given to the infants did not affect the type of intestinal bacteria. Each diet apparently resulted in a characteristic flora.

There was a marked difference in flora within twenty-four hours when the infant was changed from breast feeding to any artificial feeding. When the diet was changed from cow's milk to breast milk, the characteristic flora did not develop for two weeks.

The nasopharyngeal flora, the bacteria present in the feedings, even in as large numbers as in fermented lactic acid milk, and parenteral infections had little apparent influence on the intestinal flora.

Rest on the metabolism bed had no obvious effect on the bacteriology of the feces.

There was some correlation between the gross appearance of the stools, the bacterial flora, hydrogen ion concentrations and total titrable acidity.

A quantity of carbohydrate, in this instance lactose, in the formula sufficient to produce the same quantitative relation between lactose and protein that exists in breast milk was apparently the important factor in determining the bacterial flora of the feces, while rest on the metabolism bed, parenteral infection, flora of the nasopharynx or bacteria contained in the feedings had surprisingly little effect on the intestinal flora in the six infants studied.

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THE SUBSTANCES INVOLVED IN THE COAGULATION OF THE BLOOD OF THE NEW-BORN

II. THE EFFECT OF ULTRAVIOLET RADIATION AND VIOSTEROL *

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AND

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It was found in a former study [1] that the values of the blood clotting elements in the new-born indicate that every factor is in favor of increased coagulability under normal conditions. Other influences must be considered to cause a change in these various components if spontaneous hemorrhage results. It was, therefore, considered advisable to test the results of various influences on these factors.

METHOD

Ten new-born infants were exposed to ultraviolet radiation by means of an air-cooled mercury vapor quartz lamp of 110 volts, 60 cycles and 10 amperes. A voltage of 70 was always administered and maintained throughout the exposure. The dorsal and ventral surfaces were exposed for two minutes each daily, and the time increased one minute a day until the length of the exposure was eight minutes.

Next, ten new-born infants were given 3 drops of viosterol in oil 250 D on the second day, and the dose was doubled each day until 96 drops was given; this dosage was used for two days.

The bleeding time, coagulation time, number of platelets, antithrombin index, prothrombin index and fibrinogen count were determined as has been previously described.

The results are summarized in tables 1 and 2.

COMMENT

As has been noted by other investigators, the bleeding time is decreased and the platelets are increased by exposure to ultraviolet

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* From the Department of Pediatrics, Rush Medical College of the University of Chicago, and the Presbyterian Hospital.

1. Sanford, H. N.; Gasteyer, T. H., and Wyat, Lois: The Substances Involved in the Coagulation of the Blood of the New-Born, Am. J. Dis. Child. **43**: 58 (Jan.) 1932.

TABLE 1.—*Blood Analysis of Daily Coagulation Factors in New-Born Infants Exposed to Ultraviolet Radiation (Average of Ten Cases)*

Age, Hours	Ultraviolet Exposure, Minutes	Clotting Time, Minutes	Bleeding Time, Minutes	Platelets	Prothrombin Index	Fibrinogen	Antithrombin Index	Clotting Index
12	0	4.5	3.0	250,000	1.89	0.635	1.54	0.635
Normal		4.5	3.0	250,000	1.85	0.624	1.48	0.659
24	2	4.0	3.0	300,000	1.0	0.637	0.842	0.770
Normal		4.0	3.0	300,000	1.64	0.527	1.07	0.970
48	3	4.5	3.0	310,000	1.5	0.754	1.57	0.983
Normal		4.5	3.5	280,000	1.72	0.634	0.97	0.968
72	4	5.0	3.0	400,000	1.25	0.639	1.08	0.881
Normal		5.0	4.0	320,000	1.78	0.684	1.25	0.944
96	5	6.0	3.0	380,000	1.0	0.610	1.0	0.613
Normal		6.0	4.0	300,000	1.15	0.680	1.31	0.596
120	6	5.0	3.0	430,000	1.25	0.812	1.25	1.128
Normal		5.0	3.5	280,000	0.95	0.592	1.01	0.556
144	7	4.5	2.5	410,000	1.0	0.512	0.94	0.550
Normal		4.5	3.0	280,000	1.11	0.704	1.02	0.766
168	8	4.0	2.0	400,000	1.0	0.731	1.25	0.832
Normal		4.0	3.0	300,000	1.06	0.534	1.04	0.544
192	...	4.0	2.5	350,000	1.0	0.621	0.92	0.612
Normal		4.0	3.0	300,000	1.05	0.570	1.04	0.576
216	...	4.0	3.0	300,000	1.0	0.637	1.0	0.637
Normal		4.0	3.0	310,000	1.09	0.516	1.01	0.566

TABLE 2.—*Blood Analysis of Daily Coagulation Factors in New-Born Infants Given Viosterol (Average of Ten Cases)*

Age, Hours	Viosterol, Drops	Clotting Time, Minutes	Bleeding Time, Minutes	Platelets	Prothrombin Index	Fibrinogen	Antithrombin Index	Clotting Index
12	...	4.5	3.0	250,000	1.78	0.618	1.35	0.618
Normal		4.5	3.0	250,000	1.85	0.624	1.48	0.659
24	3	4.0	2.0	280,000	0.90	0.533	1.25	0.911
Normal		4.0	3.0	300,000	1.64	0.527	1.07	0.970
48	6	4.0	3.0	300,000	1.0	0.729	1.0	0.701
Normal		4.5	3.5	280,000	1.72	0.634	0.97	0.968
72	12	6.0	3.5	280,000	1.0	0.769	1.0	0.776
Normal		5.0	4.0	320,000	1.78	0.684	1.25	0.944
96	24	6.0	3.0	400,000	1.25	0.566	0.68	1.587
Normal		6.0	4.0	300,000	1.15	0.680	1.31	0.596
120	48	5.5	3.0	410,000	1.0	0.475	3.0	0.475
Normal		5.0	3.5	280,000	0.95	0.592	1.01	0.556
144	96	4.5	2.0	350,000	1.0	0.574	1.0	0.574
Normal		4.5	3.0	280,000	1.11	0.704	1.02	0.766
168	96	4.0	3.0	250,000	1.0	0.695	1.0	0.695
Normal		4.0	3.0	300,000	1.06	0.534	1.04	0.544
192	..	4.0	3.0	400,000	1.5	0.649	0.84	1.078
Normal		4.0	3.0	300,000	1.05	0.570	1.04	0.576
216	..	4.0	3.0	200,000	1.0	0.555	1.0	0.555
Normal		4.0	3.0	310,000	1.09	0.516	1.01	0.566

rays.[2] In our experiments, the prothrombin was consistently lower than the normal value until the fifth day; at this time it was considerably higher, but it fell to a lower value thereafter. The antithrombin was lower than the normal value except on the third and the sixth day. The fibrinogen was definitely increased throughout the period of the exposure, and this increase was sufficient to double the clotting index on the sixth day. The values still remained higher than normal after the exposures were stopped. As nothing was added to the system to cause this increase, obviously the ultraviolet radiation must in some way stimulate the formation of fibrinogen and prothrombin. This stimulation may be somewhat similar to the action of whole blood injected intramuscularly into a new-born infant suffering from hemorrhagic disease. Obviously, the small amount of blood injected could not furnish sufficient coagulation elements to balance the system, but its virtue of increasing coagulation must be due to some sort of stimulation to the various coagulation elements.

In the viosterol series the results were similar to those obtained with ultraviolet irradiation, but they were much more irregular. The fibrinogen was affected to the greatest degree, being consistently high, but the effect wore off rapidly even with much larger doses. On the fifth day, the clotting index was increased more than when the ultraviolet ray was used, however, not by an increase in fibrinogen but by a decrease in antithrombin. This was immediately followed by a compensatory increase in antithrombin, which reduced the clotting index below the normal value.

CONCLUSIONS

Either exposure to ultraviolet radiations or the administration of viosterol 250 D, or both, will, in the new-born, tend to increase the fibrinogen of the coagulation substance to a slight extent, and to decrease the antithrombin, thereby increasing the tendency for the blood to clot.

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2. Vannfalt, K. A.: Action de la luminère ultraviolette sur la composition du sang humain, Compt. rend. Soc. de biol. **101**:610, 1929. Sooy, J. W., and Moise, T. S.: Treatment of Idiopathic Purpura Hemorrhagia by Exposure to Mercury Vapor Quartz Lamp, J. A. M. A. **87**:97 (July 10) 1926. Sanford, H. N.: The Effect of Ultraviolet Light on the Blood of the New-Born Infant, Am. J. Dis. Child. **33**:50 (Jan.) 1927.

THE SUBSTANCES INVOLVED IN THE COAGULATION OF THE BLOOD OF THE NEW-BORN

III. THE EFFECT OF WITHHOLDING PROTEIN AND FAT FROM THE DIET *

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AND

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It was found in a former study [1] that in the normal new-born outside influences must be considered to cause a change in the blood clotting elements, if spontaneous hemorrhage results, as in the normal new-born infant every factor is in favor of increased coagulability under normal conditions. For this reason the following procedure was followed.

PROCEDURE

Ten new-born infants were given nothing but 5 per cent dextrose and Ringer's solution for the first five days of life. They were then breast fed, and the following day the usual complementary feeding was given.

The bleeding time, coagulation time, number of platelets, antithrombin index, prothrombin index and fibrinogen were determined as has been previously described.

The results of the experiment are given in the accompanying table.

COMMENT

There was an increase in the clotting time, but no change in the bleeding time during this period. The platelets were slightly decreased during the period of no feeding and slightly increased when feeding was begun. There was a slight decrease in the prothrombin and no appreciable change in the antithrombin. There was definite decrease in the fibrinogen, which reached a low value on the sixth day. It increased above normal following the giving of breast and supplementary feeding.

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* From the Department of Pediatrics, Rush Medical College of the University of Chicago, and the Presbyterian Hospital.

1. Sanford, H. N.; Gesteyer, T. H., and Wyat, Lois: The Substance Involved in the Coagulation of the Blood of the New-Born, Am. J. Dis. Child. **43**:58 (Jan.) 1932.

In our series, the decrease in fibrinogen was the greatest factor. It was sufficient to lower the clotting index below normal for the first five days, being most marked on the fifth day, when it was markedly below the normal value. It was not thought advisable to continue withholding breast and supplementary feeding beyond the fifth day, as an intense jaundice and slight cyanosis with red blood cells in the urine developed in one of the infants. The clotting time of this infant's blood rose to ten minutes. All the symptoms disappeared when breast and supplementary feedings were given.

Schloss and Commisky,[2] in a study of the blood in hemorrhagic disease, found in one case a deficiency of thrombin and in another case

Blood Analysis of Daily Coagulation Factors in New-Born Infants on a Nonprotein Diet (Average of Ten Cases)

Age, Hours	Feeding	Clotting Time, Minutes	Bleeding Time, Minutes	Platelets	Prothrombin Index	Fibrinogen	Antithrombin Index	Clotting Index
12	5% dextrose	4.5	3.0	250,000	1.77	0.637	1.39	0.644
	Normal	4.5	3.0	250.000	1.85	0.624	1.48	0.659
24	5% dextrose	5.0	3.0	280.000	1.14	0.559	1.0	0.559
	Normal	4.0	3.0	300,000	1.64	0.527	1.07	0.970
48	5% dextrose	6.0	3.5	300,000	1.05	0.605	1.03	0.655
	Normal	4.5	3.5	280,000	1.72	0.634	0.97	0.968
72	5% dextrose	6.0	5.0	300,000	1.04	0.651	1.0	0.651
	Normal	5.0	4.0	320,000	1.78	0.684	1.25	0.944
96	5% dextrose	7.0	4.0	280,000	1.2	0.600	1.18	0.609
	Normal	6.0	4.0	300,000	1.15	0.680	1.31	0.596
120	Breast	8.0	2.5	320,000	1.0	0.438	1.0	0.438
	Normal	5.0	3.5	280,000	0.95	0.592	1.01	0.556
144	Breast and supp.	6.5	2.0	340,000	1.0	0.477	1.0	0.477
	Normal	4.5	3.0	280,000	1.11	0.704	1.02	0.766
168	Breast and supp.	4.0	2.0	310,000	1.0	0.607	1.0	0.607
	Normal	4.0	3.0	300,000	1.06	0.534	1.04	0.544
192	Breast and supp.	3.0	2.0	320,000	1.0	0.645	0.88	0.659
	Normal	4.0	3.0	300,000	1.05	0.570	1.04	0.576
216	Breast and supp.	3.0	2.0	310,000	1.0	0.570	1.0	0.570
	Normal	4.0	3.0	310,000	1.09	0.516	1.01	0.566

a deficiency in fibrinogen. Whipple[3] also found a deficiency of prothrombin in a case of hemorrhagic disease in the new-born, as did Gelston[4] in three cases. The observed and studied results of an analysis of the coagulation factors in hemorrhagic disease of the new-born, therefore, point toward a deficiency of prothrombin or of fibrinogen as a causative factor. Both these factors are increased when adult whole blood is injected into the new-born system, and the coagulation becomes normal.

2. Schloss, O. M., and Commisky, J. J.: Spontaneous Hemorrhage in the New-Born, Am. J. Dis. Child. **1**:216 (March) 1912.

3. Whipple, J. H.: Hemorrhagic Disease, Arch. Int. Med. **12**:637 (Nov.) 1913.

4. Gelston, C. F.: On the Etiology of Hemorrhagic Disease of the New-Born, Am. J. Dis. Child. **22**:351 (Oct.) 1921.

Hemorrhagic disease of the new-born was formerly not an uncommon condition; now it is exceedingly rare. There has not been a single instance of hemorrhagic disease in our service for new-born infants in two years. For the past two years, it has been a routine feeding procedure to offer the new-born a supplementary feeding of two-thirds milk and one-third water, with 6 per cent dextrimaltose, within four hours after birth. The dietary factor in hemorrhage has been discussed by several authors.[5]

The ten infants were given 5 per cent dextrose and Ringer's solution, ad lib., during the first five days, and fever or more than normal loss of weight did not develop in any of them. Ample salts and carbohydrates were furnished by the dextrose and Ringer's solution, but the infants were deprived of fat and protein, as furnished by the mother's milk and supplement of cow's milk. When these food elements were given, the fibrinogen increased to more than normal value. It would therefore appear that dietary factors, namely fat and protein, as furnished by breast milk and cow's milk, affect the function of coagulation.

CONCLUSIONS

Withdrawal of fat and protein from the new-born, as furnished by breast milk and a supplementary feeding of cow's milk, tends to decrease the fibrinogen of the coagulation substance and thereby to decrease the power of the blood to clot.

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5. Whipple, J. H., and Foster, D. P.: Blood Fibrin Studies, Am. J. Physiol. **58**:379 (Jan.) 1922. Moore, C. U.; Broodie, J. L., and Hope, R. B.: Effects upon Young of Inadequate Maternal Diet, ibid. **82**:350 (Oct.) 1927. Kugelmass, I. N., and Samuel, E. L.: Dietary Protein and Blood Clotting Function, Am. J. Dis. Child. **41**:48 (Jan.) 1931.

SERUM THERAPY IN MENINGOCOCCUS MENINGITIS *

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While the intrathecal administration of serum in meningococcus meningitis has been fairly satisfactory as generally practiced, it has been hoped that a method might be devised that would provide a larger initial dosage and a wider distribution of serum. In the spring of 1926, I attempted to do this by introducing serum into the spinal subarachnoid space and into the ventricles, following this immediately by drainage from the cisterna magna until the flow from the needle practically stopped. In the three patients I treated in this manner [1] the results were very gratifying. Each patient received two such treatments thirty-six hours apart, and no more serum was required to keep the fluid free from organisms after the third day. Early and complete recovery occurred.

In February, 1930, I removed a complicating obstruction of the aqueduct of Sylvius [2] by means of injecting serum into the cisterna magna and withdrawing fluid simultaneously from the right ventricle. In discussing this work with Dr. E. A. Park in March, 1930, he remarked that Dr. L. H. Weed had suggested that it might be advantageous to give larger doses of serum by introducing the serum into the ventricle and simultaneously withdrawing fluid from the spinal subarachnoid space. This seemed to me an improvement over the method that I had employed.

EXPERIMENTAL DATA

I tried the procedure on the cadaver of a 9 months old baby. One cubic centimeter of Dandy's neutral solution of phenolsulphonphthalein (the monosodium salt solution) was added to normal horse serum, and it was possible to introduce 60 cc. into the ventricle before any dye appeared in the fluid that was being simultaneously withdrawn from the spinal subarachnoid space. Very gentle suction on the needle introduced into the lumbar region was aided by gravity in the syringe to the ventricle, and the procedure offered no mechanical difficulties.

CASE 1.—Shortly afterward, a case of meningitis in a child, aged 10 months, presented itself, and while the laboratory studies on the purulent fluid were being made, 60 cc. of serum was introduced into the right ventricle, and fluid to the extent of 70 cc. withdrawn simultaneously from the spinal subarachnoid space. There was

* Submitted for publication, June 17, 1931.

1. Lyon, G. M.: Epidemic Meningitis, West Virginia M. J. **26**:385 (July) 1930.

2. Lyon, G. M.: Probable Aqueduct Obstruction Occurring in Meningococcus Meningitis, J. A. M. A. **95**:109 (July 12) 1930.

no untoward reaction, and the child acted in a manner similar to that of one having received the usual dosage of from 10 to 20 cc. of serum by intraspinal injection alone. This had hardly been completed when the laboratory reported pneumococci in the spinal fluid. The serum did not, of course, influence the early fatal outcome.

CASE 2.—In May, 1930, I treated a boy, aged 12 months, with a patent and bulging anterior fontanel, as will be described. A lumbar puncture was done, and purulent fluid containing gram-negative diplococci was recovered. A right ventricular puncture was made. The barrel of a 100 cc. Luer syringe served as a serum reservoir. Rubber tubing and an adapter connected this syringe with the needle to the ventricle. To the antimeningococcus serum in the syringe was added 1 cc. of neutral phenolsulphonphthalein. The gentle pressure of gravity was permitted. Then lumbar puncture was done, and a 100 cc. Luer syringe was attached to the lumbar puncture needle through rubber tubing. Very gentle suction (barely more than the weight of the plunger) was applied at the latter site, and 70 cc. of purulent fluid was withdrawn before the dye from the serum appeared. Meanwhile, 55 cc. of serum had been admitted into the right ventricle. Both syringes were disconnected from the needles, and the fluid pressure was essentially normal after approximately 2 cc. had dripped from the lumbar needle and less than 0.5 cc. from the ventricular needle. The child had no untoward reaction, and was more comfortable after the operation than on admission. Then there was a sharp rise in temperature, and after from four to five hours, signs of increasing intracranial pressure developed, and he was relieved of 15 cc. of fluid by lumbar puncture at the end of six hours. This procedure was repeated for the same indications at the end of fourteen, twenty-six and thirty-eight hours following the administration of the serum. There were practically no organisms on the smear at the end of thirty-eight hours, and the cultures at that time were negative. The same procedure of serum administration was repeated at the end of the fiftieth hour, and 60 cc. of serum was introduced into the left ventricle and 78 cc. of fluid removed from the spinal subarachnoid space. Spinal drainage was repeated four, twelve, twenty-four, twenty-six, forty-eight, sixty, seventy-two, ninety-six and one hundred and thirty-two hours after the second administration of serum. No organisms were obtained on smear or culture from any of the fluids obtained fifty or more hours after the initial serum administration. The temperature was below 100 F. (rectal) seventy-two hours after the second administration of serum, and never rose above that. The patient had an uneventful, uncomplicated recovery, and was perfectly normal one year later. He received a total of 110 cc. of serum in two administrations.

CASE 3.—In June, 1930, a girl, aged 13 months, had a patent and bulging fontanel. She was given two such serum treatments, receiving 65 cc. at the first and 75 cc. at the second, forty-eight hours later. No organisms were found in smear or culture in the fluid after thirty-six hours following the first administration of serum. The fluid was examined at eight-hour intervals to determine, if possible, the time at which fluid sterilization occurred. Positive cultures were not obtained after twenty-eight hours nor positive smears after thirty-six hours. These had irregular gram-staining characteristics, and their morphologic and staining characteristics suggested a markedly diminished viability, if there was any viability at all. The patient's temperature was under 100 F. (rectal) on the fifth day after the first injection of serum, and she had a rapid and uneventful recovery. She was normal one year later, the time of writing this paper.

CASE 4.—In March, 1931, I treated another patient, a severely prostrated boy, aged 10 months, who had had marked meningeal signs for three days before admission. The fontanel was patent, bulging and tense. This was a more severe case

than either of the preceding two. The patient was so comatose that he did not resist lumbar puncture. The cerebrospinal fluid contained gram-negative diplococci. A needle was inserted into each ventricle, and a 50 cc. Luer syringe barrel was attached to each needle by means of rubber tubing. Each barrel was filled with serum containing neutral phenolsulphonphthalein. Lumbar puncture was then done with the patient on his left side, and 76 cc. of serum was admitted before the dye appeared. The syringe barrels to the ventricles were held at the same level, and so the serum level and pressure remained the same. Approximately 90 cc. of purulent fluid (containing possibly some serum) was withdrawn from the spinal subarachnoid space. The left ventricular needle was withdrawn first, and the pressure allowed to return to normal, approximately 1 cc. escaping from the right ventricular needle and 3 cc. from the spinal subarachnoid needle. The patient continued to be prostrated for the first twelve hours, but by the end of twenty-four hours a remarkable change had occurred, and he was greatly improved as to sensorium. His temperature remained around 103 F. continuously for five days. Pressure was relieved by lumbar puncture four, eight, twelve, eighteen, twenty-four and thirty-six hours after the first serum treatment, and the serum treatment was repeated as before at the end of forty-eight hours. He received 100 cc. of serum at the second administration, and approximately 120 cc. of fluid was withdrawn from the spinal subarachnoid space, the last 10 cc. containing some dye. No cultures were positive after the first thirty-six hours. Some intracellular diplococci were found at the end of fifty-six hours after the first serum treatment (eight hours after the second), but growth was not obtained after the first thirty-six hours. Frequent drainage by lumbar puncture was done to relieve pressure, from 15 to 20 cc. of fluid being taken at a time. The temperature came down gradually after the fifth day following the first serum treatment. The patient's general clinical improvement was rapid and progressive, so that by the end of the first week he had practically recovered. He is apparently well at the time of writing.

Case 5.—Owing to a mistaken laboratory report, a second case of pneumococcus meningitis was treated in much the same manner. At the time the case was reported by the laboratory to be meningococcus meningitis, but subsequent examination of the fluid proved the error of this report. In this case, an infant, aged 9 months, with a patent and bulging fontanel, extremely prostrated and comatose, was treated in the following manner: Lumbar puncture was done first, and the 100 cc. Luer barrel containing serum and dye was attached. Then, with the patient lying on his left side, a left ventricular puncture was done, a 100 cc. Luer syringe attached, and gentle suction applied. Only 60 cc. of serum was available. All of it was introduced, and 80 cc. of purulent fluid was withdrawn simultaneously from the left ventricle. As yet no dye had appeared in the fluid from the ventricle. The syringes were detached from the needles, the pressure allowed to approach normal, and the needles withdrawn. Left ventricular puncture thirty minutes later for the relief of pressure showed the dye to have reached the ventricle. During the twelve hours following this procedure, the baby took feedings for the first time in thirty-six hours. This is cited to show that the child, even in this prostrated condition, was not further depressed by this rather radical procedure. The child died of pneumococcus meningitis eighteen hours after admission, four days after the onset. This was the only patient in the series to have serum introduced into the spinal subarachnoid space and fluid withdrawn simultaneously from the ventricle.

Case 6.—The fourth patient with meningococcus meningitis to be treated in this series was a boy, aged 3½ years. Because of the unusual features in this case, such as our inability to sterilize the spinal fluid with available serums, the occurrence of

an Arthus phenomenon,[3] etc., the case will merely be referred to, and will be reported in detail later. It may be said, however, that, following signs of a ventricular obstruction during the second week of the boy's illness, a trephine opening was made, the ventricles tapped, a reservoir containing antimeningococcus serum and dye attached to each ventricular needle, and fluid withdrawn from the spinal subarachnoid space. This procedure was repeated several times a week for a period of three weeks. From 80 to 100 cc. of fluid was removed from the spinal subarachnoid space at a time, and from 70 to 100 cc. of serum introduced simultaneously into the ventricles. I refer to this case here in order to show that the procedure may be done repeatedly on a patient. There was at no time a more severe reaction than that which usually accompanies spinal or ventricular administration of serum. This may be difficult to believe, unless one has actually witnessed it. The patient died subsequently, because it was impossible to obtain a serum that would sterilize the cerebrospinal fluid.

COMMENT

In retrospect, these patients showed no untoward effects from the procedure. Vomiting, convulsions, cardiac and respiratory embarrassment or bizarre serum phenomena did not occur in any of the cases cited, except in the last patient referred to. The injudicious use of pressure in the intraspinal administration of serum would seem to be fraught with greater risk than the procedure here reported, in which pressure is gentle, and there is always a relatively safe pressure from gravity alone at the serum reservoir, with very gentle suction at the site of fluid withdrawal. By allowing pressure to return to normal after the administration of serum, one does not leave the serum under increased pressure. An increased output of cerebrospinal fluid occurs after the introduction of serum, just as in spinal subarachnoid therapy, and as pressure increases it must be relieved by drainage.

In the fifth case cited, I attempted to administer the serum from below, as it had been suggested that there might be danger of jamming the brain stem into the foramen magnum if there was too much suction below or an obstruction of the aqueduct. The serum can be administered either way. I prefer having the double serum reservoir attached to the ventricles with withdrawal from the spinal subarachnoid space.

SUMMARY

While, admittedly, the series reported here is too small from which to draw any conclusions, there are certain factors worthy of further consideration.

1. The cerebrospinal fluid became sterile within from thirty-six to forty-eight hours. This, of course, has happened on single injections of smaller doses of active serum intraspinally, and can be only suggestive, not conclusive.

3. Dr. H. L. Amoss has also witnessed such an occurrence (personal communication).

2. These patients, given but two injections of serum, received very large doses of serum at each injection; in this respect the desideratum was approached, i. e., a high concentration of serum in the cerebrospinal fluid with a chance for maximum and speedy toxin neutralization, agglutination, bacteriolysis and phagocytosis, and a wide distribution of the serum throughout the cerebrospinal fluid system.

3. A child of 9 months took from 60 to 70 cc. of serum at one administration. A child of 3½ years took from 90 to 100 cc. The major portion of this serum remained within the cerebrospinal fluid system, even if from 10 to 20 cc. more fluid was removed than was introduced. This gives some idea of the amount of serum that may be substituted for cerebrospinal fluid by this method of serum administration or "substitution."

4. The method has not been severe on the patients so treated, and unfavorable reactions have not occurred. The patients have been singularly free from increased depression or other untoward effects, such as one might anticipate from such a form of treatment.

5. Clinical improvement has been remarkably speedy and satisfactory in cases of meningococcus meningitis, except, of course in the case of the patient whose infection was refractory to all serums tried. No obstructions occurred, except in the case that was refractory to serum.

6. The amount of cerebrospinal fluid in a child of 9 months would seem to be in excess of from 60 to 70 cc., and in a child of 3½ years in excess of from 90 to 100 cc., probably from 15 to 20 per cent more.

7. This method is particularly valuable in the case of an infant with a patent anterior fontanel. In such cases it may be employed with ease. In infants the incidence of complications and the mortality rate is usually highest.

8. Because of the decreased number of administrations of serum, and the shorter period of serum therapy made possible by this method, the chances of an Arthus phenomenon occurring would be greatly reduced.

CONCLUSION

This method of substituting serum for cerebrospinal fluid is presented with the realization that such a small series of cases cannot be more than suggestive of possible results. It is a method that may be employed with relative safety to the patient. It makes possible a greater dosage and a wider distribution of serum than may be had with other methods. It should be effective in preventing, as well as removing, complicating obstructions. This method should produce a higher percentage of complete recoveries, and quicker recovery than any method of serum therapy now in use.

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THE INFANT WARD*

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My subject may seem both simple and stale. And yet, to one who knows the hazards, and has on his conscience the responsibility for the conduct of an infant ward, it is never either of these. An infant mortality that, in our experience, is easily four times that of the whole Children's Memorial Hospital, and seven times that of the children beyond the age of 18 months, is a constant challenge. Some of this mortality is inevitable; there is no cure for tuberculous meningitis or congenital atresia of the esophagus. Nor is there need to be so deeply concerned if this mortality represented only the futile efforts to overcome a disease with which the child entered the hospital if there is no better way to meet the situation elsewhere. The specter of an institutional casualty, more insidious and less evident here, but far more real than elsewhere, sits always with us at our board. No amount of habit and tradition would ever seem to be able to lead us to become calloused to this most unhappy of all medical experiences. It has seemed to me worth while to call attention to the dangers that are inseparable from massed institutional care of sick infants, to discuss the causes that underlie the high morbidity and mortality, and to consider some remedial measures that naturally suggest themselves.

When we come to consider the causes of this high morbidity and mortality, both intrinsic and institutional, those of us who have practiced over twenty-five years are impressed with the fact that there has been a significant change in etiology, and a resultant change in therapeutic point of view. There has been a very evident shift from the gastrointestinal tract to the respiratory tract, with diarrhea and indigestion as prominent symptoms common to both. The term "summer complaint" was no idle misnomer in those days. "Summer complaint" occurred during the summer. It was enteral, not parenteral. We were not concerned in our infant wards, as we are now, with respiratory infections, with ears and with mastoids and pneumonia, and we were as interested in those things then as we are now. For a time I attended an old-fashioned foundling home. The mortality was nearer 100 per cent than 50 per cent. The babies nearly all had intractable diarrhea,

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and we were rarely aware of any parenteral infection. In the infant wards we spent weeks and months trying to get marantic babies, with or without diarrhea, to accept our scientific aims and ideals, and to profit by them. The high peak of morbidity and of mortality was in the late summer. Last year at the Children's Memorial Hospital our lowest infant attendance was in July; the lowest mortality in August, 7 per cent as compared with the annual infant mortality of 27 per cent. The highest occupancy was roughly from September to April, inclusive, with a roughly corresponding mortality curve, except that it was shifted about one month to the right. In about 50 per cent of the deaths the cause was ascribed to bronchopneumonia, and in a much higher percentage infection of the respiratory tract was an important factor. The percentage of deaths due apparently to enteral causes, in which, at least, we were unable to discover a parenteral factor, was very low, except that during the third quarter of the year there was a distinct rise, with, however, still a very low relative mortality. There was a corresponding rise in attendance during September, probably due to the same causes that prevailed years ago. There was not a single transmission of a so-called contagious disease during the year.

Whether the cause of the greater rôle of respiratory infections today lies in an actual greater incidence and (or) greater virulence of these infections, or whether there is merely a relative preponderance due to the receding incidence of primary gastro-enteral disorders that naturally followed advances in infant feeding and hygiene may be problematic. I feel strongly that there is a significant increase both in number and in virulence. Be that as it may, I do not think that one can justly postulate a single common etiology for the gastro-intestinal disorders and intoxications that are common to both enteral and parenteral disease. Neither do I think that one is justified in assuming that an identical therapy was indicated then as now. The feeding problem was the main thing in that earlier period, partly because of the nature of the disorders that had to be dealt with, partly, probably largely, because of lack of knowledge of how to meet them. Today it is relatively incidental, as is evident from the chaotic simplicity and multiplicity of equally vaunted and apparently nearly equally effective fool-proof therapeutic foods, of which sauer kraut juice, milk and scraped raw apple are, at this writing, so far as I know, the latest. The poker spirit that now obtains is shown in the fact that when Moro recently advocated the exclusive use of from 1 to 3 pints of scraped raw ripe apple a day for diarrhea in children, some one in the discussion of his paper immediately raised his ante by indicating a preference for green apples.

The thing that worried us years ago, and still does, was what was called "hospitalism," and there was much speculation as to

its causes. It certainly was not then, and is not now, wholly covered by, or co-extensive with, parenteral infection. I think it was Czerny who found monotony, staring at blank walls and ceilings, an important factor. The absence of "mothering" ranked high, and I think still should. It was a common observation that "nurse's pet" got along better than the rest. We used to have a rule that every baby should be picked up, carried around, amused and "mothered" several times a day. I, myself, had an idea, that I think was well founded in those days, that a determining difference between the care of the ward baby and the home baby lay in the fact that the one got immediate attention when there was a change for the worse, while the other, owing to hospital routine, or what not, often went from twenty-four to forty-eight hours before a change in food that seemed indicated was carried out, and then commonly by an inexperienced intern. A great change came with the advent of special therapeutic foods. The introduction of protein milk (Eiweiss milch) changed the whole aspect of pathologic infant feeding. The younger man will never fully appreciate, as some of us do, the debt of gratitude that we owe to Finkelstein and his co-workers. Today the major cause of "hospitalism," if that term may be expanded, lies in infections of the respiratory tract and their complications. The baby that enters with such an infection is apt to get worse; the baby that enters for some other condition is almost sure to acquire such an infection if it stays long enough; and in infant wards these infections manifest a morbidity and a mortality that have no approach to a parallel condition in the home, in the private room or anywhere else.

Why are these infections so much more beyond control than the ordinary so-classed contagious diseases, and why are they so much more destructive than they are in the home? Some factors, at least, seem evident. The common contagious diseases have a fairly constant, stereotyped course and degree of severity, and are readily recognizable. We know the period of incubation and something about the duration of contagiousness. Patients with the mildest and the severest contagious disease, and those with the mildest and the severest form of each disease are treated exactly alike so far as isolation is concerned. Equally important, these diseases have a tradition—they are "contagious" and are so treated. Every one is on the lookout for the earliest symptoms so that immediate isolation and quarantine can be established. They are, moreover, largely restricted to the patients themselves—transmission from attendants is of minor importance. In contrast to all this, respiratory infections may vary all the way from an afebrile running nose, cough or scratchy throat to a tonsillitis or septic sore throat; all of these occur just as freely among attendants as among the patients themselves, with a resulting enormous increase in contacts. There is no well established protective tradition; no useful knowledge as to degree

or duration of contagiousness, and any and every one of these infections, whether in a child or in an attendant, may transmit a fatal infection to the type of infant that is found in infant wards. So long as nurses are allowed only a very limited number of days of sick leave annually, it is too much to expect of human nature that they will at once report every cold or sore throat, and it is not yet heavily traditional that such infections are a serious enough menace to warrant withdrawal from the ward and crippling of the hospital service. The intern, too, who is surrounded by respiratory morbidity and mortality and is loath to miss anything, cannot fully appreciate that his cold or cough or sore throat may add materially to the situation, especially if he wears a white coat and pants. The attending physician, too, apparently has sometimes much the same feeling of harmlessness, especially if he wears a more distinctive, longer white coat, with black buttons all the way down the front.

Theoretically, at least, it seems to me, too, that it is just as reasonable to think in terms of "carrier" here, as has long been done, I think rather overdone, in the prophylaxis of diphtheria, and as is now being done in some places in that of scarlet fever. Whereas only about 5 per cent of persons have diphtheria germs in their throats, Kendall told me that he had found streptococci in 100 per cent of 653 throats during the World War. Helmholz has found at times 100 per cent of hemolytic streptococci in the throats of normal children. In a recent appraisal of all of the attendants in the Children's Memorial Hospital, 105 out of 225 had hemolytic streptococci in their noses or throats. Julianelle found hemolytic streptococci in 90 per cent, staphylococci in 62 per cent and green-producing streptococci in 31 per cent of extirpated tonsils. All of these organisms are probably less pathogenic from normal throats than from those they have infected—but who knows to what extent this is true? It is known what the streptococcus did in concentration camps during the World War. One is constantly aware of what it does in the infant ward under similar conditions of herding and of massed contact. The pneumococcus and the staphylococcus and others are there also, but in minor rôles. Whether these organisms are brought in by patients and spread directly and indirectly from patient to patient, or whether they come from attendants, from special strains, from cough droplets or from dust; from allergic sneezes, tobacco coughs and contaminated handkerchiefs, gowns, hands or face masks; from the sick or from carriers, may make little difference; it is reasonable to assume, as is done in surgery, that a million loose streptococci, staphylococci or pneumococci will more readily take root, and take root more deeply, than will a few. There are millions of these in infant wards, and there is apparently a most favorable soil for their reception and development. A lowered resistance to the invasion and spread of

these infections here can be assumed a priori, is supported by experience, and is rather confirmed by the fact that it finds no approach to a parallel in wards for older children, in the home, or in maternity wards where babies are even far more closely crowded together.

While massed exposure and low resistance would seem the important factors in this condition, there are other angles that may be significant. The sick infant lies helplessly in one position, usually on his back. Approximately 50 per cent of the deaths in the Children's Memorial Hospital last year occurred in babies under 4 months of age, and nearly 75 per cent in those under 7 months. At autopsies on marantic infants, one finds almost constantly a disseminated bronchopneumonia, or at least a broad longitudinal band of pneumonia corresponding to the most dependent part of the lung in the dorsal position—a real pneumonia, not merely a congestion, or livores. Nearly all of these infants with parenteral infections have gastro-intestinal disorders and vomit to some extent—commonly a great deal. These babies cannot have sufficiently constant care so that they can be turned over quickly enough to avoid aspiration of vomitus. They can hardly be trusted to lie on their stomachs as a well baby can. May this not possibly be an important factor, not only in the genesis of bronchopneumonia, as compared with lobar pneumonia, but also in that of otitis media? The eustachian tube is relatively patulous and very short in infancy, and is possibly even more permeable in dehydrated or emaciated infants. It seems to me not wholly unreasonable to think that when such an infant lies on its back and vomits, so that the whole pharynx and nasopharynx are filled with fluid under pressure, some of the vomitus will gain entrance to the middle ear and may cause an otitis media. There are times when 90 per cent of our babies have an otitis media, and it is by no means always possible to determine the presence of a causal infection of the throat, as can so readily and regularly be done under more normal conditions.

In recent years the mastoid antrum has been brought into relief as an important, even, at times, the most important, factor in the causation of the severe gastro-intestinal disorders and intoxications that occur in hospitalized infants. It has long been a matter of common observation that 50 per cent or more of infants that die in infant wards from almost any cause, and especially those that have severe gastro-intestinal disorders, are found at autopsy to have pus in the mastoid antrum. It is hard to see how otitis media can fail to invade the mastoid antrum when one considers the anatomic relations. It has always seemed to me, both a priori and from experience, that such invasion is an effect, or a coincidence, and only rarely a cause in itself of distant pathology and symptomatology. The answer can be found only in a striking, unquestionably resultant and fairly constant therapeutic effect from anthrotomy as compared with myringotomy. Much evidence has been

advanced that there is such a therapeutic effect. In our experience at the Children's Memorial Hospital it has been quite wanting. Perhaps we have delayed too long. In the few cases in which we have not delayed too long we have been unable to convince ourselves that the course of the disease has been significantly changed for the better, and when the termination was favorable we were unable to exclude coincidence. We have thought rather of the underlying respiratory infection, including perhaps the otitis media and the invasion of the antrum, *together with the resulting or accompanying gastro-intestinal disorder itself,* as *the* determining factors.

Be all these things as they may, the important facts that confront us and that lie on our conscience are that there is a very high morbidity and mortality in infant wards; that this is today largely due to infections of the respiratory tract, which are in part brought in by the patient and in part acquired after entrance, and that in both instances conditions tend to become seriously aggravated by the unfavorable influences inherent in an infant ward. It is evident, too, if these things are true, that prophylaxis alone offers any large measure of relief. Some of these measures would seem obvious and can be stated categorically and dogmatically:

1. No patient should be admitted to an infant ward who can with reasonable assurance be taken care of in an outpatient department, or in a good home or foster-home. Our own infant wards of 30 beds in a 285-bed hospital are rarely full, often only half full, and at times get down to six or seven patients. Only about 10 per cent of our patients are under 18 months of age. Especially to be excluded are boarders and infants with infections of the respiratory tract and gastro-intestinal disorders that are not immediately serious. More can be done in an outpatient department than is commonly assumed. I might cite the experience of Kassowitz, who treated fifty children with empyema by rib resection in an outpatient department without hospitalization and with a mortality of 6 per cent, the lowest that I know of. A visiting intern, or resident physician, and a Ford, also suggest themselves.

2. Every infant should be dismissed as soon as convalescence has set in and he can safely be taken care of elsewhere. In the Children's Memorial Hospital we have an arrangement by which such infants come back for a time in the outpatient department, to the attending physician, intern and resident physician who have had them in charge in the hospital, before returning to the general clinic. It is, unfortunately, not an uncommon experience to have babies return in a short time, as bad or worse than they were before. It is what might be expected from the homes in which the condition arose in the first place. Ideal here, from every standpoint, is the foster-home idea, so humanely conceived and so efficiently carried out by Dr. Chapin in the

Speedwell Plan and, following his leadership, by others in other places. The hospital that has no such plan is seriously handicapped and is not doing its full duty, either medically or financially. The convalescent home is not a full substitute; it does not eliminate herding at a dangerous age.

3. An adequate and efficient social service is a sine qua non, both to furnish information about the home and also to get the child out as quickly as possible and to follow him into the home after he is discharged. Equally important is a close, constant and sympathetic cooperation of the medical staff with the social service.

4. With 37 per cent of our deaths occurring within the first twenty-four hours of hospitalization last year, it is evident that at least that number represented real emergencies. This point has been so persistently emphasized by Dr. Clara Davis, who had charge of our infant wards last year, that we have hurdled routine and repeated examinations and have sometimes had babies in their cribs within twelve minutes of the time they entered the dispensary. This probably accounted, at least in part, for a reduction in deaths within twenty-four hours after admission from 41 per cent of all deaths in the first six months to 33 per cent in the second six months of last year. Such emergency service, too, makes no distinction between day and night, with a special allotment of interns if necessary.

5. One nurse to two babies should represent a minimum.

6. All attendants in an infant ward should have constantly the state of mind toward all possible contagion that the surgeon has toward a flaw in asepsis. Contagion-mindedness should become habitual and traditional, as it is in contagious wards, and should automatically include such things as washing the hands between patients, especially if they have come in contact with the patient's mouth or nose; a change of gown to a fresh one after each suspicious contact; the changing of sheets between each two patients on an examining table; the avoiding of all dry sweeping and unnecessary shaking of sheets and bedding, and the use of individual toilet articles, thermometers, etc., at the bedside. Long sleeves would seem clearly objectionable for either interns or nurses, especially those of interns' coats, which are starched and cannot be rolled up and are worn all day. Ideal are gowns with long sleeves with knitted ends that will completely cover any underlying sleeve, on the one hand, and can be pushed above the elbow with full assurance that they will stay there. I think that the wristwatch should also be taboo. As in all contagion, probably the greatest factor here, too, is the immediate contact of donor and recipient. Patients must not come near one another, and all attendants, nurses, interns and attending physicians with acute respiratory infections should be excluded

from infant wards for the time being. I am dubious about the efficacy of face masks. While cubicles are doubtless of value, I think that they are a bit disappointing in this type of infection, and have the disadvantage of poor ventilation. Especially desirable is a separate ward for all patients who are free from infections, analogous to the clean surgical ward.

7. An equable temperature, neither too high nor too low, nor too abruptly changeable, is of great importance, as is also a proper regard to humidity.

8. Finally, sick, debilitated, emaciated infants with subnormal temperatures should be scrupulously guarded against chilling from exposure, bathing, etc; from excessive and frequent handling and examining, and from overzealous therapy. Babies are neither cold-blooded nor fur-bearing animals, and chilling is not a negligible factor in the production and aggravation of respiratory infections. The ritual bath is commonly more honored in the omission than in the commission. The intern and the resident are eager to learn; there are many of them, and both they and the attending physician are anxious to make a correct diagnosis, and often many and long examinations are made on an exposed infant. It is better practice to permit a baby to get well without a diagnosis than to have a meticulous, scientific diagnosis confirmed at autopsy. Dr. Robert Preble, an internist with a very large fund of hard-boiled common sense, once told me that there was one time in his life that he could treat pneumonia as he thought it should be done. During the World War, after the diagnosis was made, he said to his assistants, "Now we know that this man has a pneumonia. Let him alone—do not examine him again unless there is an obvious change that requires it." If this was true of men fitted for army service, how much more so for infants whose lives often hang on a thread.

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ROENTGENOGRAPHIC CHANGES IN THE THORAX OF NORMAL PREMATURE BABIES

A DAILY ROENTGENOGRAPHIC STUDY OF FIFTEEN NORMAL PREMATURE BABIES DURING THE FIRST FOURTEEN DAYS OF LIFE *

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Since 1925, when Johnson and Meyer [1] called particular attention to pneumonia of the new-born, the diagnosis of this and other intrathoracic conditions of this period has been much more frequently made, and the most helpful diagnostic aid has been the roentgenogram.

In a previous communication we [2] demonstrated the usefulness of a series of roentgenograms of the thorax of full term, normal infants taken daily during the first fourteen days of life. Briefly, such control observations were helpful in the interpretation of films taken when infants suffered from unexplained cyanosis or cyanotic attacks, from disturbances of respiratory rate or rhythm, from varying degrees of collapse, and the like, in other words, when pneumonia of the new-born or any other intrathoracic lesions was a possible cause of the disturbance. Since one meets such puzzling situations in premature babies even more frequently than in full term infants, it is the more desirable to know how to interpret any films taken for purposes of diagnosis. So far as we could ascertain no control study has been reported.

We therefore made daily bedside roentgenograms of the thorax of normal premature babies for the first fourteen days of life. These infants were born in the obstetrical service of the Long Island College Hospital, and the mothers had been followed by the prenatal clinic. If there was cyanosis, feeble cry, dyspnea, excessive loss of weight or any

* Submitted for publication, June 1, 1931.

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1. Johnson, W. C., and Meyer, J. R.: A Study of Pneumonia in the Stillborn and Newborn, Am. J. Obst. & Gynec. **9**:151 (Feb.) 1925.

2. Weymuller, C. A.; Bell, A. L. L., and Krahulik, L.: Roentgenographic Changes in the Thorax of Normal New-Born Babies, Am. J. Dis. Child. **35**:837 (May) 1928.

other symptom suggestive of abnormality, the films were excluded from this series. Only one infant was cyanotic at birth, and required artificial resuscitation. This situation cleared up immediately, and the infant was normal at all subsequent examinations. Nearly thirty babies were studied before we were able to collect fifteen completely controlled series of fourteen films each. We selected babies under 2,500 Gm. in

TABLE 1.—*Summary of Clinical Status of the Fifteen Normal Premature Infants Studied*

Patient	Birth	Birth Weight, Gm.	Days in Hospital	Course in Hospital	Type of Delivery	Cause of Prematurity
Tor.	June, 1929	2,180	22	Uneventful; cyanosis and difficult resuscitation at birth	Cesarean section	Unknown
Par.	June, 1929	1,840	14	Uneventful	Spontaneous, left occipito-anterior position	Unknown
Rub.	July, 1929	1,620	18	Uneventful; tube-fed	Spontaneous, left occipito-anterior position	Nephritic toxemia
But.	Aug., 1929	2,140	14	Uneventful	Spontaneous, right occipito-anterior position	Doubtful history of syphilis unproved
Gig.	Nov., 1929	2,160	52	Uneventful; tube-fed	Spontaneous, right occipito-anterior position	Unknown
Rag.	Dec., 1929	2,220	39	Uneventful; systolic murmur P^2 on discharge and thereafter	Spontaneous, right occipito-anterior position	Unknown
Lis.	Feb., 1930	1,900	16	Uneventful	Spontaneous, right occipito-anterior position	Unknown
Bon.	Feb., 1930	2,200	13	Uneventful	Spontaneous, left occipito-anterior position	Unknown
Mal.	March, 1930	2,160	14	Uneventful	Spontaneous, left occipito-anterior position	Unknown
Kel.	April, 1930	1,520	48	Uneventful; tube-fed	Spontaneous, right occipito-anterior position	Toxemia cardiac
Rom. A	April, 1930	1,800	27	Uneventful	Spontaneous, breech position	Multiple pregnancy
Rom. B	April, 1930	1,820	27	Uneventful	Spontaneous, left occipito-anterior position	Multiple pregnancy
Bla.	June, 1930	2,040	18	Uneventful	Spontaneous, left occipito-anterior position	Hepatic toxemia
Fal.	Feb., 1931	2,240	14	Uneventful	Spontaneous, right sino-anterior position	Unknown
Boy.	April, 1931	2,120	14	Uneventful; tube-fed 8 days	Spontaneous, left occipito-anterior position	Unknown

weight, regardless of body length, because all babies under 2,500 Gm. require the same care as premature babies, and seem fully as susceptible to serious disturbances. Our smallest baby was 1,540 Gm. (3 pounds and 6 ounces), the largest 2,200 Gm. (4 pounds and 14 ounces), and the average weight was 1,930 Gm. (4 pounds and 4 ounces). The type of delivery and the suspected causes for the infants' small size were so variable as to seem insignificant to us.

TECHNIC

We found that these roentgenograms of the thorax could be made with practically no handling and necessitated no restraint, since these infants were practically motionless. In fact, the films were made with a portable bedside unit, without removing the infant from the incubator. The factors used were 88 peak kilovolts; 30 milliamperes, and 25 inch (63.46 cm.) distance. The exposure time was one tenth of a second. The patient was placed in the supine position, and an attempt was made to make the films at the height of inspiration.

FINDINGS

Pulmonary Markings.—In general, the lung fields were much clearer than those of full term infants. There was a characteristic delicacy of structure of all of the lung markings in the premature

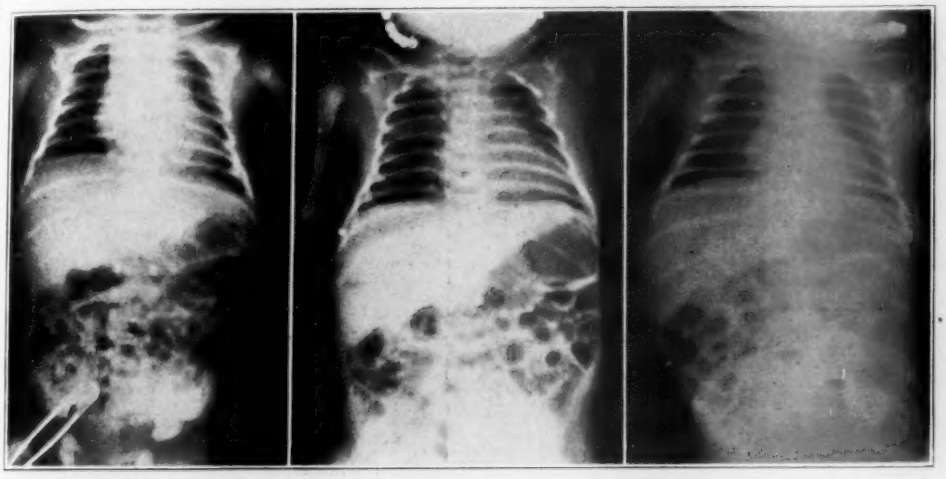

Fig. 1.—Normal premature boy on the first, second and fourth days. Note the characteristic delicacy of the lung markings with strikingly diminished density. There was little change from day to day; the interlobar pleural line is not visible.

infants, and in eight of the series this delicacy of structure produced strikingly diminished densities of the lung fields. Whereas most of the full term infants showed increased hilar and peribronchial markings on the first and second days with a gradual tapering off, this was true of but three of fifteen premature infants. Furthermore, there was so little change from day to day in the premature series that practically any film might be chosen as characteristic. It is well known that these peribronchial and hilar shadows are cast by the bronchi, lymphatics, connective tissue and blood vessels, and that the chief factor in the production of these shadows is the blood vessels. It therefore seems reasonable to believe that the decreased density and more delicate struc-

TABLE 2.—*Roentgenographic Observations of Fifteen Normal Premature Infants*

Patient	Birth Weight, Gm.	Pulmonary Fields	Cardiac Shadow	Mediastinum
Tor.	2,180	Typical delicate hilar and peribronchial densities, most marked on first day, decreased slightly each day	Little or no change in size; left border became more concave after fifth day	No noteworthy changes
Par.	1,840	Typical delicate hilar and peribronchial densities first two days, more dense on third day, average after fourth day	Left border enlarged on first day; average size after second day	No noteworthy changes
Rub.	1,620	Increased densities of hilar and peribronchial shadows for first two days, decreased gradually to average picture after fourth day	No noteworthy changes	No noteworthy changes
But.	2,140	Typical delicate hilar and peribronchial densities until sixth day; peribronchial mottling right upper lobe from sixth to fourteenth day; interlobar pleural line seen on third day film and several others	Little change in size; left border convex on first day, less on second day, average contour by fifth day and thereafter	No noteworthy changes
Gig.	2,160	Typical delicate hilar and peribronchial densities uniformly seen	Little change in size; slight fulness of left border on first day; average contour on second day and thereafter	No noteworthy changes
Rag.	2,220	Typical delicate hilar and peribronchial densities uniformly seen	Definite enlargement to the right on first day; less on second and third days; average size thereafter with fulness of right border persistent; left border unchanged	No noteworthy changes
Lis.	1,900	Typical delicate hilar and peribronchial densities uniformly seen	Upper cardiac shadow markedly increased on first day; narrowed progressively to sixth day; average size from sixth to ninth days, thereafter broader upper borders than average, except on eleventh day when size was normal for this series	No noteworthy changes
Bon.	2,200	Typical delicate hilar and peribronchial densities uniformly seen	Little change in size or contour	No noteworthy changes
Mal.	2,160	Typical delicate hilar and peribronchial densities uniformly seen	Slight gradual diminution in size after second day; slight fulness of left upper border on first three days	No noteworthy changes
Kel.	1,520	Typical delicate hilar and peribronchial densities uniformly seen	Little change in size or contour	No noteworthy changes
Rom. A	1,800	Hilar and peribronchial densities unusually delicate until tenth day, thereafter average picture for a premature infant	Enlarged on first day; progressively smaller to fifth day; on fifth day unusually small; size average thereafter; no change in contour	Broad shadow in upper third for first three days, thereafter average width, probably due to position
Rom. B	1,820	Typical delicate hilar and peribronchial densities after first day; first day markings very indistinct	Enlarged on first day; average on second day, thereafter unchanged	Somewhat widened until sixth day; thereafter average

TABLE 2.—*Roentgenographic Observations of Fifteen Normal Premature Infants—Continued*

Patient	Birth Weight, Gm.	Pulmonary Fields	Cardiac Shadow	Mediastinum
Bla.	2,040	Linear markings very indistinct on first day, thereafter average delicate density of hilar and peribronchial regions	Unusually full left border on first day; average size by third day; unchanged thereafter	No noteworthy changes
Ful.	2,240	Typical delicate hilar and peribronchial densities first four days; more dense than average until eighth day; thereafter average	Slight enlargement on first day, average on second day; thereafter unchanged	No noteworthy changes
Boy.	2,120	Typical delicate hilar and peribronchial densities first day; even less dense on second and third days; more dense than average on tenth, eleventh and twelfth days	Some enlargement on first day, especially right-sided; smaller on second day and average size after third day	Upper mediastinal shadow slightly broader than average on first and sixth days, apparently due to position
Maximum	2,220	Hilar and peribronchial shadows uniformly delicate in structure and much less dense than in full term infants	Cardiac shadow diminished slightly after the third day; less striking than in full term infant; fulness of left border during first three days was frequently noted	Practically no change noted in this region
Minimum	1,520			
Average	1,980			

ture of the peribronchial trunks observed in these premature babies is accounted for by the relatively smaller size of the blood vessels.

In only one subject (baby But.) was the interlobar pleural line between the right upper and middle lobes demonstrable. This line was quite regularly found in normal, full term infants, and it varied with position. It is interesting that this patient was one of the largest of the infants studied, weighing 2,200 Gm. (4 pounds and 14 ounces). This finding leads one to wonder whether the weight of the patient determines the density of these tissues, and whether there may be a weight level beyond which this common finding for larger babies may be found. These observations are numerically insufficient to warrant a conclusion.

Heart Shadows.—It is to be remembered that most of the full term infants showed definitely larger cardiac shadows on the first and second days. The size of the cardiac shadow diminished and became fairly constant in size after the third day. This was in general true of the premature infants studied, although the changes in size were much less striking. In only three patients was the heart shadow uniform throughout. In two patients the enlargement of the first day persisted until the fifth and sixth days. When there was decided enlargement (six cases) during the first three days, the fulness was most marked at the left border. While the changes in size were not striking, the changes in cardiac contour were almost constantly present. They were manifested

as increased fulness and convexity of the right and left borders on the first day, followed by diminution in the fulness of the right border plus straightening, and finally convexity of the left border. In all but two cases these changes in contour occurred during the first three days.

Of special interest was baby Rag. There was definite alteration in the shape of the right side of the heart, in addition to the enlargement common on the first day. This was manifested as a fulness of the right atrial region. At this time no murmurs were heard, although they were particularly listened for. After the first day, the left border of the

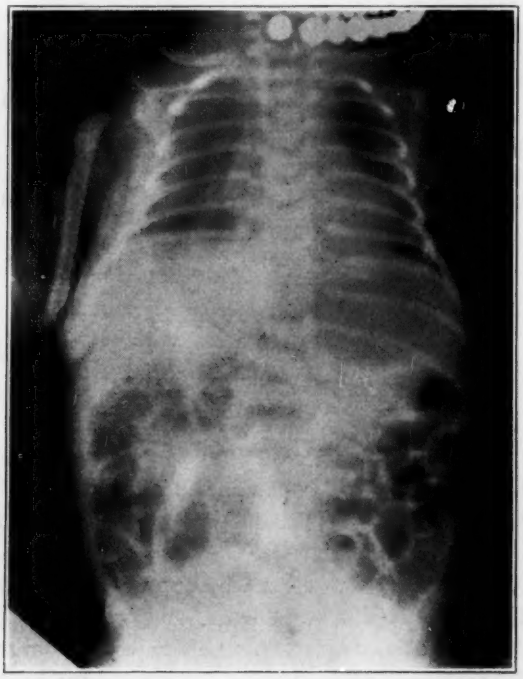

Fig. 2.—Normal premature boy on the eleventh day. Note the characteristic delicacy of the lung markings with strikingly diminished density. There is little change from the films of earlier days; the interlobar pleural line cannot be seen.

heart diminished in the average manner, but the fulness of the right atrial region persisted. On the fourteenth day, a definite systolic murmur transmitted to the vessels of the neck was heard over the region of the pulmonic second sound. This murmur persisted in the same intensity on all subsequent examinations. The latest examination was made when the infant was 8 months of age. There was no cyanosis or other sign of circulatory disturbance. Although this particular lesion had apparently done no harm, another of our patients who succumbed to congenital heart disease on the thirty-seventh day showed no more

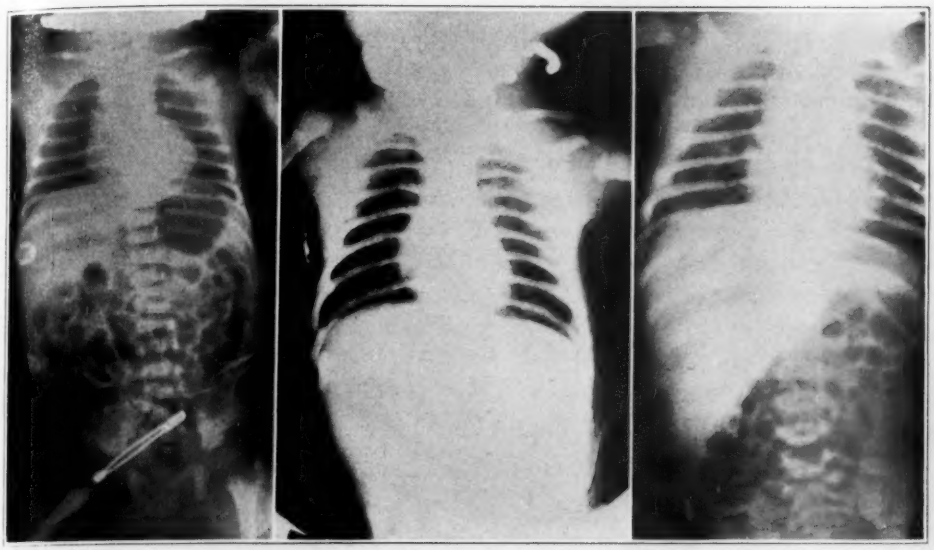

Fig. 3.—Comparison of the roentgenograms of the thorax of a normal premature infant, a normal full term infant and an infant who had pneumonia neonatorum. There is sharp contrast between the very slight density in the premature infant, the plainly defined linear markings of the normal, full term infant and the mottling and heavy density of the infant with pneumonia.

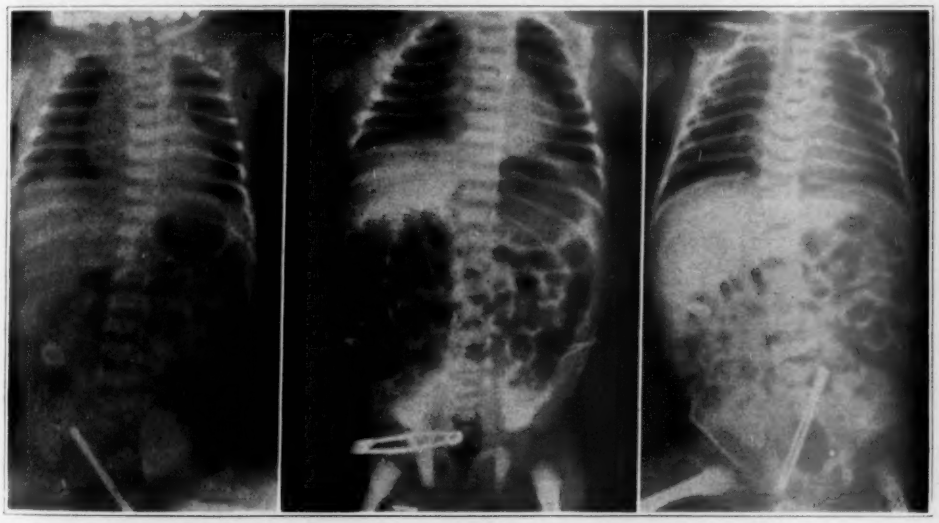

Fig. 4.—Normal premature boy on the first, third and fifth days. The size of the cardiac shadow diminished only slightly; the right and left borders flattened perceptibly after the third day, quite regularly.

disturbance than this during the early days of life. Obviously, one must conclude that evidence of congenital heart lesions is not always present on the initial examination, and that potentially serious lesions can easily be overlooked, unless repeated clinical observations and roentgenographic studies are made.

Mediastinum.—There was variation in the mediastinal shadow in but one instance, in contrast with the decided variation in those of full term infants. Baby Rom. A showed a wide upper mediastinal shadow on the first and second days. Thereafter the shadow was of average width for premature infants. Since respiratory excursion is so slight

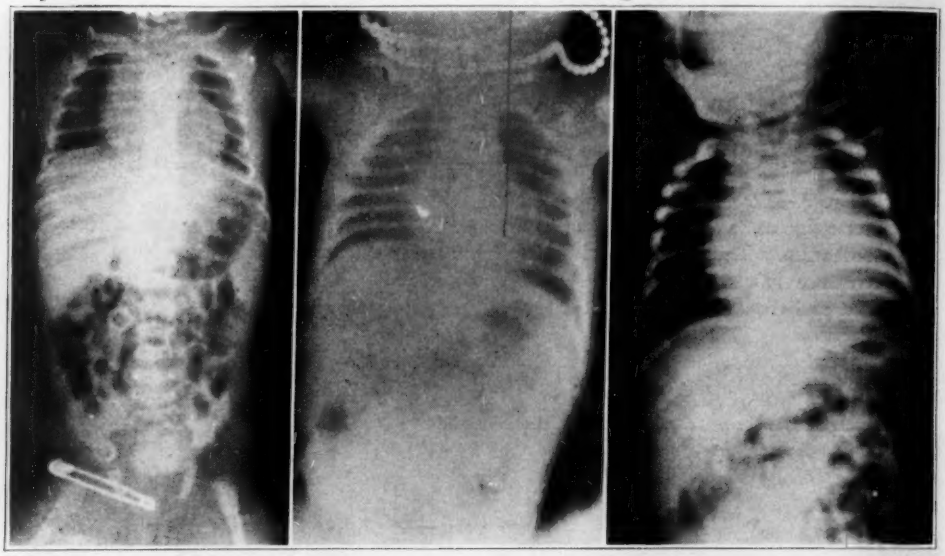

Fig. 5.—The cardiac shadow of baby Rag. (left), who had a congenital heart lesion of little consequence, differed little from the early picture of baby Fag (middle) who succumbed to coarctation of the aorta. A later film of Rag. is shown at the right of this group. Heart murmurs could not be heard during the early days. The value of the roentgenogram in early diagnosis and follow-up is obvious.

in premature infants the reason for the lack of variation in mediastinal shadow is clear.

COMMENT

The findings were generally similar to those for the full term infants, except that the pulmonary fields, hilar and peribronchial trunks were much less dense and the peribronchial shadows were more delicate in structure. They were clearer the tinier the baby. In but one instance did we find the interlobar pleural line which was so commonly seen in full term infants, and this was observed in one of the largest

babies studied. We found no roentgenographic evidence of atelectasis, although these infants should have been promising subjects. It was interesting to note, too, that the three tiniest babies who were tube-fed for varying periods of time showed no clinical or roentgenographic evidence of the aspiration of foreign material. The heart shadows generally diminished after the second day, as in the full term infant, although three were unaltered in size during the fourteen days studied. Baby Rag. proved the importance of the roentgenogram in the diagnosis of congenital heart lesions, since there was roentgenographic evidence for days before there were ascultatory findings. This experience likewise suggests that no definite statement as to the heart of an infant should be made during the very early days of life.

There were no noteworthy changes in the upper mediastinal shadow of any of these infants. In fact, nothing suggestive of thymic enlargement or mediastinal glandular enlargement was seen.

We believe that the roentgenogram of the thorax can be of great help in disclosing the cause of serious disturbances suffered by premature infants, especially the seldom identified pneumonia of the newborn. The interpretation of films taken will be aided by study of a control series or review of the observations made in this series.

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ATELECTASIS IN THE NEW-BORN*

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Atelectasis in the new-born is the abnormal persistence of the condition of incomplete expansion of the lungs which is physiologic in the first few days of life. The lungs of the fetus are completely atelectatic. With the onset of respiration expansion begins, but, as pointed out by Wasson,[1] in most cases it probably does not become complete for several days. A certain amount of atelectasis is physiologic, therefore, during the first few days of life, but ordinarily does not cause symptoms. When it is sufficiently extensive to cause symptoms, it must be regarded as pathologic.

In cases of atelectasis in the new-born, failure of proper functioning of the respiratory center is generally held to be the most frequent cause of abnormal persistence of the fetal state in some parts of the lungs. Often the cause of the failure of the respiratory center cannot be determined, but immaturity, asphyxia, hemorrhage of the brain or edema may be responsible for the condition. Mechanical factors, such as plugging of a bronchus by mucus or pressure on the lung by an enlarged heart or, possibly, by an enlarged thymus gland, are said to cause atelectasis of the lungs occasionally in the new-born infant. Atelectasis of the lungs in the new-born infant is therefore never primary but always secondary to some condition that interferes with the mechanism bringing about full expansion of the lungs.

The chief symptom of atelectasis is cyanosis, which may be constant or intermittent. Other symptoms, such as a weak cry, rapid, shallow, irregular breathing and cough may be present, but their association with atelectasis is not constant. The physical signs of atelectasis may be definite or they may be confusing. The characteristic fine, crepitant râles are often missed because the infant is not stimulated to take a deep inspiration. If the atelectasis is sufficiently extensive, the percussion note may be impaired, and the breath sounds may be diminished or bronchial. If, however, the atelectatic area or areas are small but scattered, percussion or auscultatory changes may be difficult or impossible to detect. As a result the severity of the symptoms may be greatly out of proportion to the signs.

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* From the United States Children's Bureau (Studies of Neonatal Morbidity and Mortality) and the Pediatric Department of the Yale School of Medicine.

1. Wasson, W. W.: A Roentgenographic Study of the Infant Chest as Seen at Birth, J. A. M. A. **83**:1240 (Oct. 18) 1924.

The diagnosis of atelectasis can be made most satisfactorily by use of the roentgenogram. This method of diagnosis has been but rarely referred to in the current literature. Grulee [2] mentioned the importance of roentgen examination to differentiate atelectasis from other conditions causing cyanosis. Rose,[3] in a recent article, drew attention to the importance of the use of roentgenograms and emphasized the scarcity of the literature on the roentgenographic picture in atelectasis. Wasson pointed out that in the interpretation of roentgenograms the angle that the ribs make with the spine is an important diagnostic sign. When the lungs are fully expanded, the ribs tend to form a right angle, while in atelectasis the angle is less.

A roentgenogram of a stillborn infant's chest shows the picture of complete atelectasis (fig. 1*A*). The chest is narrow and cone-shaped rather than barrel-shaped, the lateral wall of the chest tends to be

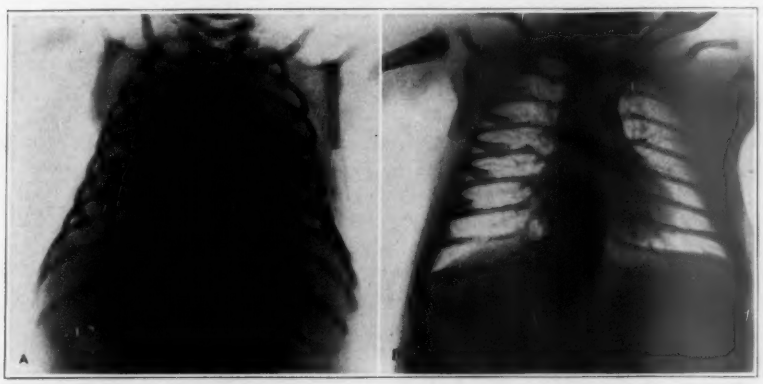

Fig. 1.—*A*, the unaerated lungs of a stillborn infant. Note the cone-shaped thorax, the concave borders of the chest and the acute angle that the ribs form with the spine. *B*, inflated lungs of stillborn infant. Note the clarity of the lung fields, the more convex borders of the chest and the elevation of the ribs to more nearly a right angle with the spine.

concave rather than convex, and the ribs tend to form an acute, rather than a right angle with the spine. Figure 1*B* shows the chest of a stillborn infant after the lungs have been artificially expanded by air. If these films are compared it is evident that after expansion the lung fields are relatively clear, the chest tends to be more barrel-shaped, the lateral chest wall more convex, and the ribs are elevated and form more nearly a right angle with the spine. This picture simulates that of the normal infant's chest when the lungs have become well expanded.

2. Grulee, C. G., and Bonar, B. E.: The Newborn: Diseases and Abnormalities, New York, D. Appleton & Company, 1926, p. 89.

3. Rose, C. B.: Persistent Congenital Atelectasis, Radiology **14**:488 (May) 1930.

REPORT OF CASES

In the course of a special study of new-born infants six cases of pathologic atelectasis were seen in which the diagnosis was confirmed by roentgenograms.[4] The case histories are as follows:

CASE 1.—M. C., a girl, was born spontaneously at term after a prolonged second stage of labor. The birth weight was 3,720 Gm. There was considerable difficulty in resuscitating the infant. Livid asphyxia was present. On examination, about four hours after delivery, the left side of the chest was impaired to percussion over the upper third, back and front. Over the whole left side the breath sounds were distant and tubular, and fine crepitant râles were present. The clinical diagnosis was extensive atelectasis of the left lung. The roentgenogram showed atelectasis of the upper two thirds of the left lung. A film taken three days later showed some atelectasis still present, but no symptoms were apparent. The infant was discharged at 12 days of age and is living and well at 2 years.

The roentgenograms in case 1 were unsatisfactory, because the infant was not held properly and the film was taken off center. They are therefore not reproduced. The only conclusion that could be drawn from the film was that nearly the whole left lung showed increased density, a picture which corresponded with the physical findings.

CASE 2.—E. C., a girl, was born spontaneously at term. The birth weight was 4,438 Gm. On the second day the infant had attacks of cyanosis accompanied the next day by choking and difficulty in breathing. On examination of the chest no changes in the percussion note or in the breath sounds were made out, and râles were not heard. The clinicial diagnosis was atelectasis in spite of the negative observations on the lungs. The roentgenogram showed definite atelectasis throughout both lungs. The symptoms disappeared twenty-four hours later, and a roentgenogram showed the lungs to be clear.

The roentgenogram taken in case 2 (fig. 2*A*) on admission shows homogeneous increased density throughout both lung fields. The density is greater on the right, the outline of the right side of the heart being practically obliterated. The diagnosis of diffuse atelectasis was strengthened by the cone-shaped thorax and the tendency of the ribs to form less than a right angle with the spine. The roentgenogram (fig. 2*B*) taken two days later shows some residue of hypoventilation. The broad mediastinal shadow with irregular outline is probably due, not to an enlarged thymus, but to incomplete expansion of the lungs. The ribs, however, have become more elevated, the chest tends toward a barrel shape and the width of the chest appears to have increased.

CASE 3.—I. S., a boy, was born at term and delivered by mid-forceps. The birth weight was 3,050 Gm. The infant was cyanotic at birth and the respirations were very rapid. Fine râles were heard at the bases of both lungs posteriorly.

4. All roentgenograms were made with the infant held in the erect posture and with a film target distance of 7 feet (213.3 cm.). Several films were taken in each case in inspiratory and expiratory phases, but in making comparisons of films care was taken to compare films taken in the same respiratory phase.

The clinical diagnosis was atelectasis. The roentgenogram showed partial atelectasis of the right upper lobe with a mediastinal shadow within normal limits. Two days later the symptoms disappeared, and the infant was discharged in good condition on the fourteenth day of life.

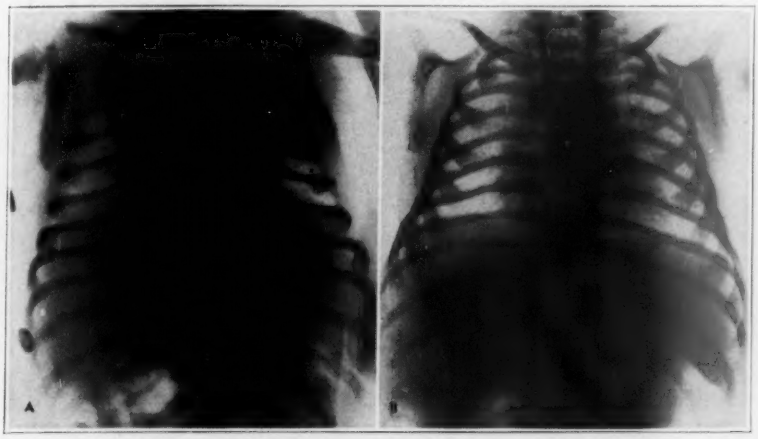

Fig. 2 (case 2).—*A*, cone-shaped thorax. Homogeneous increased density of lung fields, especially in the upper and central portions. *B*, relatively clear lung fields; elevation of the ribs; change in the shape, and increase in the size of the thorax.

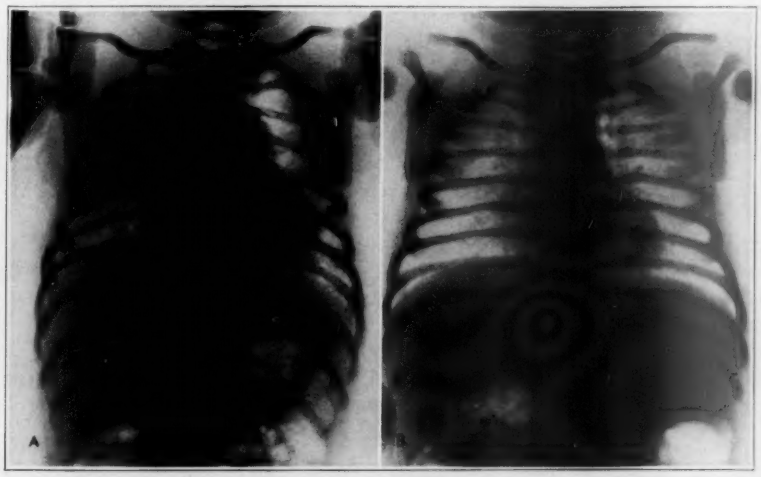

Fig. 3 (case 3).—*A*, definite area of increased density in the right upper portion, with some mottling at the right and left bases. *B*, relatively clear lung fields and elevation of the ribs.

The roentgenogram in case 3 (fig. 3*A*) shows a more localized type of atelectasis than was shown in figure 2*A* (case 2). The upper part

of the right lung is dense and there is considerable mottling of the lower part, while the left lung appears to be relatively clear. There is no shift of the mediastinum to the right, but there is a slight elevation of the right diaphragm. There is moderate angulation of the ribs, but it does not appear to be more marked on the right than on the left. The chest is narrow and slightly cone-shaped. The contrast with the appearance in figure 3*B*, taken two days later, is striking. The clarity of the lung fields, the elevation of the ribs to a right angle, the assumption of a barrel shape, and actual increase in the width of the chest are evidence of improved expansion and ventilation.

CASE 4.—A. M., a boy, was delivered at term by version and extraction after a difficult labor. The birth weight was 3,240 Gm. The infant did not breathe well. The cry was infrequent and weak. Carbon dioxide and oxygen [5] were administered in the delivery room to stimulate respirations. The right lung was dull to percussion over the upper part, anteriorly and posteriorly; over this area fine râles were heard on inspiration. The clinical diagnosis was atelectasis. The roentgenogram showed atelectasis involving the right lung. On the second day the infant's condition was good and he was discharged on the nineteenth day.

The roentgenogram taken in case 4 (fig. 4*A*) shows slight clouding of the entire right lung. The exposure was made with the body of the infant slightly rotated, which accounts for the prominence of the mediastinal shadow on the left. The shadow in the lower half of the right lung became less marked five hours after the first film (fig. 4*B*), indicating a more nearly normal degree of ventilation of the lung. The density, however, increased again on the following day (fig. 4*C*). On the second day of life the lungs were essentially clear except for slight clouding of the apexes (fig. 4*D*).

CASE 5.—O. P., a girl, was born spontaneously at home. Since the mother had severe postpartum hemorrhage resulting in her death, little attention was given the infant for some time after birth. It was then noted that the infant was cyanotic, and that the cry was weak. On admission to the New Haven Hospital, about twelve hours later, the infant was extremely cyanotic, and the temperature was subnormal (34.6 C. [94.3 F.]). The weight on admission was 4,120 Gm. The breathing was irregular, shallow and slow. The infant did not cry, but emitted an occasional feeble moan. Carbon dioxide and oxygen were administered immediately, after which the breathing improved. Subsequent examination of the lungs revealed no abnormal signs. That evening the infant had a severe attack of cyanosis, but responded again to inhalations of carbon dioxide and oxygen. The clinical diagnosis was atelectasis. There was no cyanosis after the second day, and the infant was discharged in good condition on the eighteenth day. The roentgenogram showed atelectasis of the left lung and moderate enlargement of the thymus gland.

5. A mixture of 5 per cent of carbon dioxide and 95 per cent of oxygen was used as a routine measure in these cases.

The roentgenogram in case 5 (fig. 5*A*) shows a broad mediastinal shadow and an area of increased density in the upper part of the left lung. The latter was regarded as due to atelectasis, while the former was interpreted as the shadow of an enlarged thymus gland. A lateral view of the chest showed that the thymus occupied a considerable portion

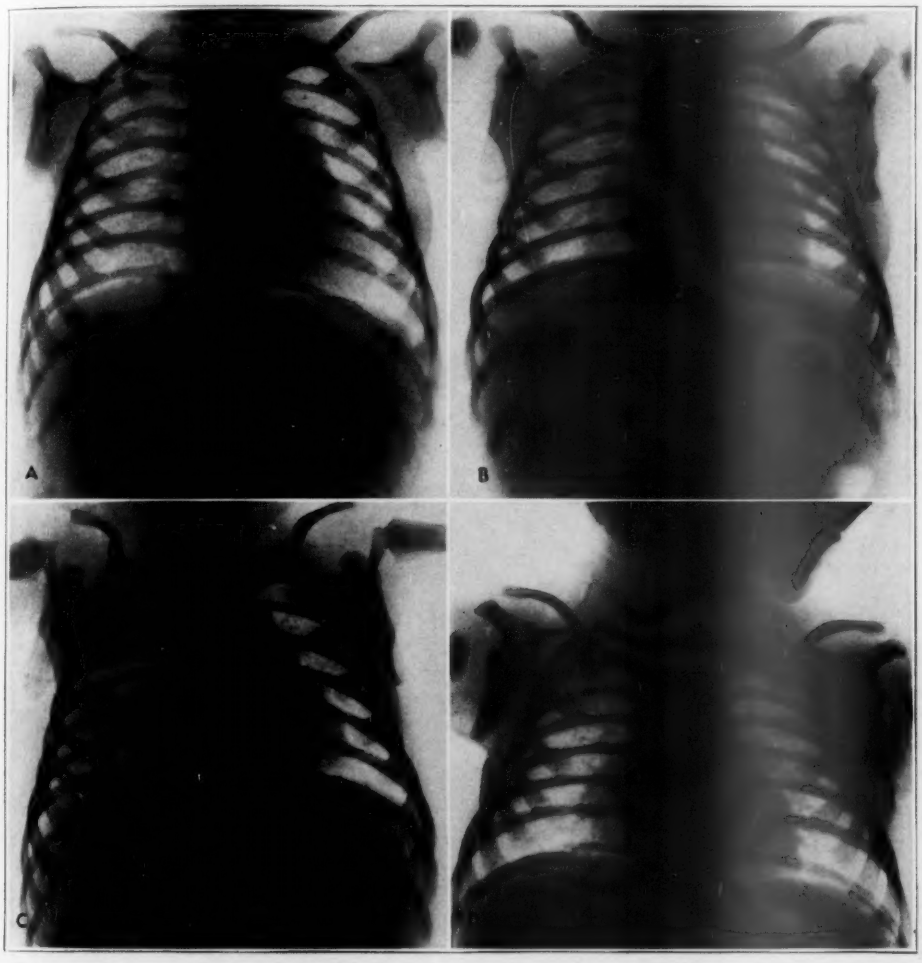

Fig. 4 (case 4).—*A*, homogeneous increased density throughout the right lung. *B*, the appearance of the lungs five hours after *A* was taken. *C*, marked increased density involving apparently the whole right side of the chest. *D*, condition of lungs in case 4 at the time of the patient's discharge from the hospital.

of the mediastinum, but there was no evidence of pressure on the trachea (fig. 5*B*). A second plate taken four days after the first showed little change, but one taken twelve days later showed the increased density in the upper part of the left lung to have disappeared (fig. 5*C*), although the shadow of the thymus gland persisted unchanged.

CASE 6.—B., a boy, was born about one month prematurely. Delivery was rapid and spontaneous. The birth weight was 3,241 Gm. It was noted immediately after birth that the infant was cyanotic and cried poorly, and that the respirations were rapid and shallow. The right side of the chest appeared normal, but over the upper part of the left lung the percussion note was impaired and the breath

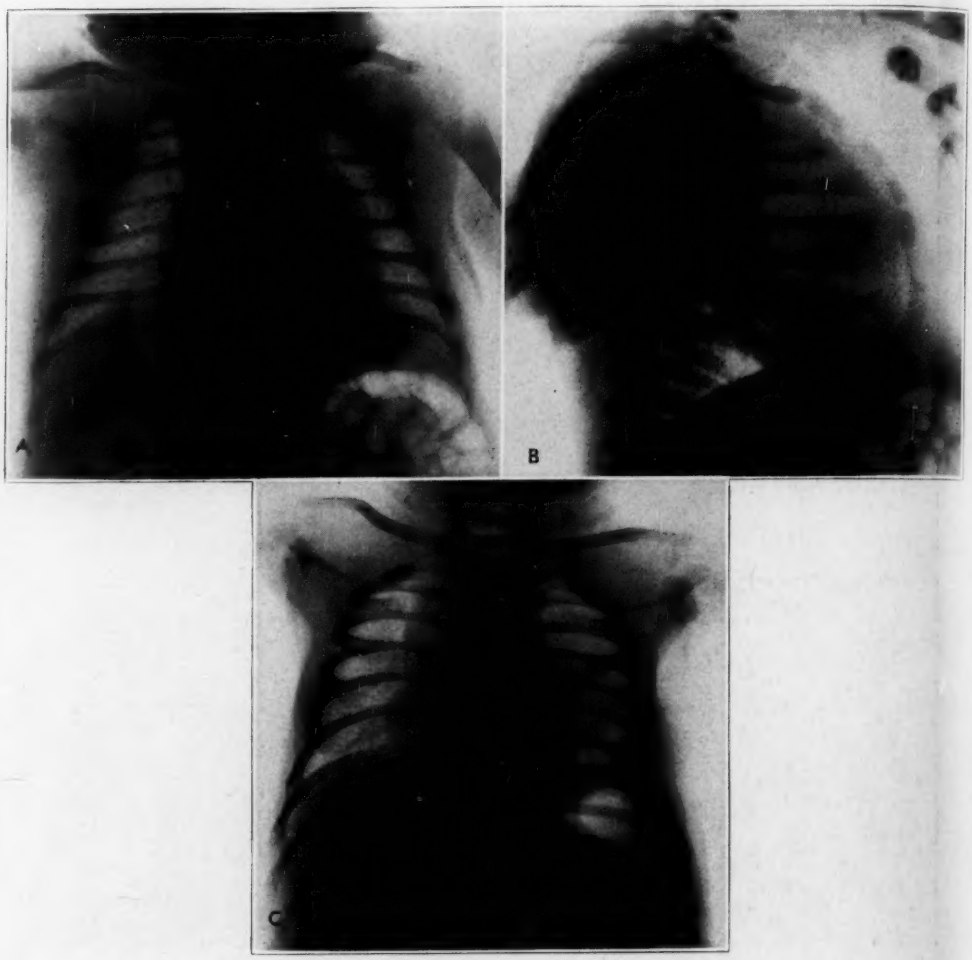

Fig. 5 (case 5).—*A*, enlargement of the upper mediastinum interpreted as the shadow of the thymus gland. Atelectasis of the upper part of the left lung is also present. *B*, lateral view of the chest shows no evidence of compression of the trachea by the thymus. *C*, the atelectatic area in the upper part of the left lung has cleared.

sounds were markedly diminished. The heart rate was rapid, and at one time a systolic murmur was audible. The spleen was palpable about two fingerbreadths below the costal margin. Carbon dioxide and oxygen were given at frequent inter-

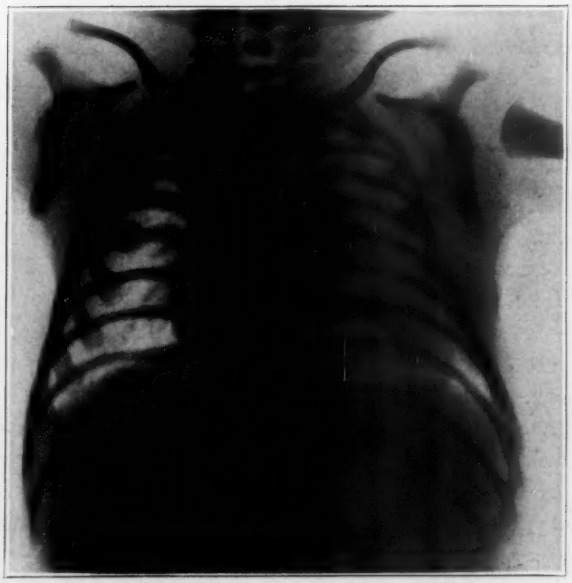

Fig. 6 (case 6).—Atelectasis of the upper part of the left lung. A seven-foot plate of the heart suggested symmetrical enlargement. The left border of the heart with the exception of the apex is obscured by the density of the atelectatic lung.

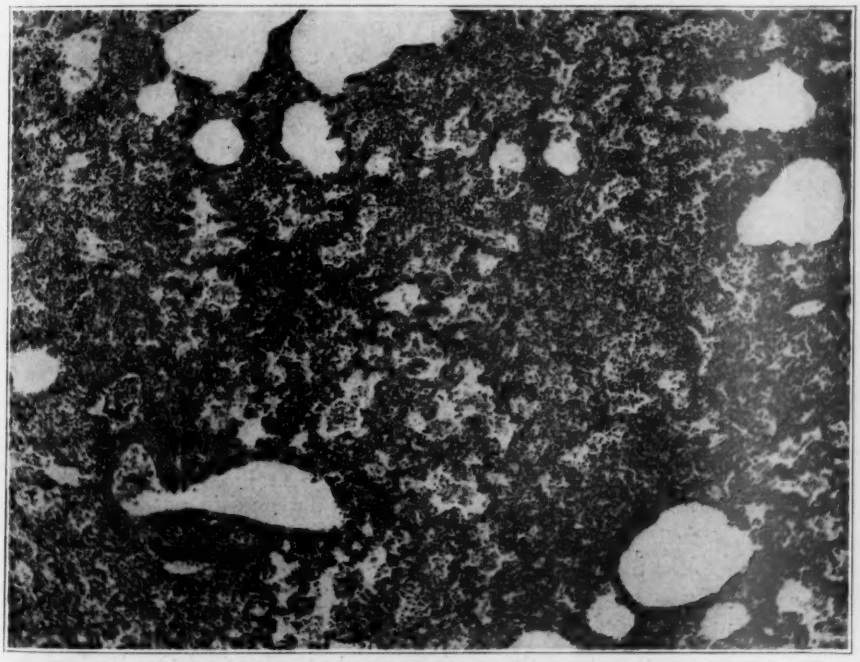

Fig. 7 (case 6).—Histologic section of the lung, showing diffuse atelectasis.

vals, but the response was poor. The infant died at the age of 30 hours. The clinical diagnosis was congenital disease of the heart or atelectasis. The roentgenogram showed partial atelectasis of the left lung with general enlargement of the heart.

The roentgenogram (fig. 6) shows what appears to be the shadow of an enlarged heart, but the upper part of the left lung appears to be atelectatic.

At postmortem examination the heart was not considered to be enlarged. The weight was about 30 Gm. The ductus arteriosus was patent and seemed to be approximately the same size as the aorta. The right and left branches of the pulmonary arteries were patent and of the usual size. There were no abnormalities of the ventricles or valves of the heart. The right lung was crepitant throughout. The left lung was dark red, firm and noncrepitant. On microscopic section marked atelectasis of the left lung was found (fig. 7). The pathologic report was: primary, pulmonary atelectasis; subsidiary, Meckel's diverticulum; patent ductus arteriosus; congestion of the viscera.

COMMENT

These six histories may be summarized as follows: All of the infants were of average or above the average birth weight. Labor was "prolonged" in one case and "difficult" in one case. In four cases the infants were delivered spontaneously and in two cases by operative procedure. Cyanosis was present at some time in every case; in five cases the respirations were abnormal; in three cases the cry was abnormal; only one infant had a cough. Signs in the lungs were noted in four of the six cases. In two cases râles were present; in three cases the percussion note was impaired over a localized area, and in two of these the breath sounds were altered over this area, in one case tubular and in the other diminished. The physical signs varied considerably from time to time. In two cases no physical signs were found, the clinical diagnosis, based on symptoms only, having been corroborated by roentgenograms.

Roentgenograms were taken in all of these cases at the time that symptoms or physical signs were present. From a study of these roentgenograms several points of importance in making a diagnosis of atelectasis may be emphasized. The lung fields may show a general haziness, and the observer may regard this appearance as due to poor technic in taking the film when it is in reality due to lack of air in the lungs. On the other hand, one or more definite areas of increased density may be seen, or only one lung may show cloudiness of greater or less intensity when the other is clear. When atelectasis involves one lung more than the other a difference in the level of the diaphragm

may be evident, the involved side not descending during inspiration as well as the unaffected side. If the atelectatic area lies in the left paravertebral region, the pulmonary change may not be visible in the films, because it will be obscured by the shadow of the heart.

SUMMARY

1. Atelectasis of the lungs in new-born infants is the abnormal persistence of the fetal state of the lungs due to some condition that interferes with the normal functioning of the respiratory center or to mechanical obstruction of the air passages.

2. The chief symptom of atelectasis is cyanosis.

3. Cyanosis due to atelectasis of the lungs can be differentiated from cyanosis caused by other conditions by means of roentgenograms.

4. The roentgenographic picture of atelectasis of the lungs in the new-born is characterized by haziness of the lung fields, which is evidence of lack of complete aeration, and by the abnormal shape of the thorax and the abnormal position of the ribs, which are evidence of incomplete expansion of the lungs.

CONCLUSION

Roentgenographic examination of the lungs is always indicated when a new-born infant is cyanotic.

ESOPHAGEAL OBSTRUCTION

A CLINICAL AND EXPERIMENTAL STUDY OF ITS EFFECT ON LIFE AND GROWTH *

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AND
THEODORE S. WILDER, M.D.
PHILADELPHIA

The effect of complete stricture of the esophagus on life and nutrition has been the subject of but few investigations. Pavlov,[1] in 1895, first mentioned the use of an esophageal fistula in the study of psychic secretion in dogs. Our impression is that few of the earlier clinicians or physiologists believed that closure of the esophagus had any serious effect on health, though this belief, as far as we can find, was not the result of experimental investigation or of clinical experience. A few years ago Wangensteen and Chunn [2] and Haden and Orr [3] recorded rapid deaths in dogs following acute experimental closure of the esophagus. Andrus and Donnelly [4] more recently have again studied the question and have concluded that the loss of saliva may have played an important rôle in the lethal outcome of all their animal experiments.

Chevalier Jackson,[5] who has had probably the largest clinical experience with benign strictures, made the observation in 1913 that the nutrition of children suffering from complete stricture markedly improved when the stricture was relieved or when saliva was mixed with the food entering the stomach through the gastrostomy opening. Carlson [6] has written us regarding one child suffering from complete stricture of the esophagus in whom the addition of saliva plus a well balanced diet improved markedly the weight and height. However, we have been able to find no record of a child in whom the addition of

* Submitted for publication, April 2, 1931.

* From the Department of Pediatrics, School of Medicine, University of Pennsylvania.

1. Pavlov, J. P., and Simanowskaja, S.: Arch. f. Anat. u. Physiol., 1895, p. 53.

2. Wangensteen, O. H., and Chunn, S. S.: Studies in Internal Obstruction, Arch. Surg. **16**:1242 (June) 1928.

3. Haden, R. L., and Orr, T. C.: J. Exper. Med. **38**:477, 1923.

4. Andrus, W. de W., and Donnelly, J. L.: Effects of Certain Operation on the Esophagus of the Dog, Including Esophageal Obstruction and Complete Esophageal Fistula, Arch. Surg. **20**:1 (Jan.) 1930.

5. Jackson, C.: Arch. Pediat. **40**:324, 1923.

6. Carlson, A. J.: Personal communication to the authors.

saliva alone without any change in the diet caused a disappearance of the malnutrition. Records of congenital cases and of patients suffering from cancer of the esophagus have been of little value because of their early lethal outcome.[7]

Any serious effect on nutrition caused by closure of the esophagus might be explained by any one or all of several hypotheses. In the first place, the salivary glands might secrete a hormone necessary to life and growth, which is not reabsorbed on account of the stricture of the esophagus. However, cases have been recorded[8] of complete absence of the salivary glands, a condition that has apparently no startling effect on the state of nutrition. In the second place, it is conceivable that the loss to the body of mineral salts secreted in the saliva and the other glandular secretions of the mouth might account for a certain amount of malnutrition. Finally, it is possible that the lack of saliva and of other secretions above the esophagus might interfere in some unknown way with the normal digestive processes of the stomach and intestines.

In order to study this problem, which is important from both a clinical and a physiologic point of view, we decided to investigate the case of a patient suffering from a complete stricture of the esophagus of seven years' duration. In addition, we felt it wise to control such an investigation by causing a smilar condition in the esophagus of a young animal, the pig, whose digestive tract so closely resembles that of man. The effect on life itself of closure of the esophagus has been studied experimentally by a few investigators with the contradictory results previously mentioned. However, the effect on growth of loss of saliva with complete stricture of the esophagus has never to our knowledge been studied by means of animal experiments. Clinical impressions in the few human cases on record have been of little value because of the lack of dietary care and supervision of the daily regimen.

REPORT OF CASE

The record of Harriet C., the subject of our clinical investigation, whom we were permitted to study through the courtesy of Dr. Chevalier Jackson, is briefly as follows:

The aunt stated that when Harriet was 2½ years old she climbed to the table and drank most of the contents of a glass which contained a solution of potash. She immediately started to cry, and vomited. The family physician washed out

7. Brennemann, J.: Atresia of the Esophagus, Am. J. Dis. Child. **16**:143 (Sept.) 1918.

8. Blackmar, F. B.: Am. J. Ophth. **8**:139, 1925. Ramsey, W. R.: Hereditary Congenital Absence of the Salivary Glands, Am. J. Dis. Child. **28**:440 (Oct.) 1924.

her stomach. She was able to drink liquids for about six months following this, when the esophagus finally closed and she was unable to swallow anything. Gastrostomy was then performed.

For a short time after this operation bougies were passed through the esophagus, after which the patient was able to swallow small amounts of fluid, but for six and one-half years previous to her admission in June, 1929, to the Graduate Hospital of the University of Pennsylvania her esophagus had been closed. A general house diet, including meat, vegetables, fruits, soups and milk, plus cod liver oil, orange juice, etc., was fed through a tube in the gastrostomy opening.

At admission, the patient was extremely malnourished considering her age of 10 years. Her weight was but 39½ pounds (17,917 Gm.). Our investigation

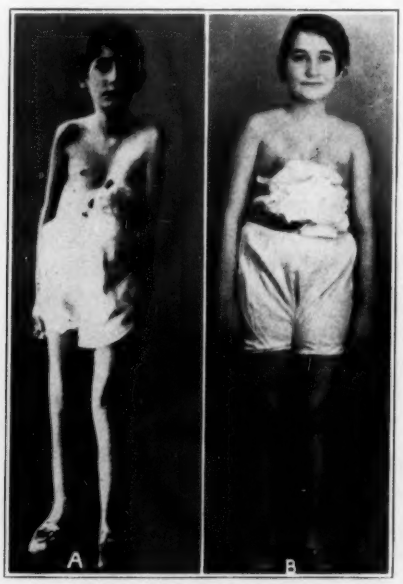

Fig. 1.—*A*, Harriet C as she appeared at the beginning of the study (weight, 37¾ pounds). *B*, as she appeared at the end of the study, after almost a year (weight, 65 pounds).

of her nutritional state did not begin until forty-eight days after her admission, when her weight had dropped to 37¾ pounds (17,233 Gm.); her height was 57 inches (144.8 cm.). The skin and mucous membranes were extremely pale; all of her teeth were dirty and carious, with a certain amount of pyorrhea. Her tonsils were large, though not obstructing her breathing. There was a small fistulous opening in the upper part of the abdomen through the left rectus muscle, just below the border of the ribs, through which a no. 16 French catheter could be introduced into the stomach. The erythrocyte count was 2,470,000, with 39 per cent hemoglobin, indicating a marked secondary anemia, while the leukocyte count was 5,700, with a differential count showing an increase in polymorphonuclear leukocytes. The red cells showed marked anisocytosis and poikilocytosis. The x-ray films taken of the esophagus on June 12, 1929, gave evidence of a

complete obstruction near the level of the suprasternal notch with a dilatation of the esophagus above this point.

Three successive retrograde examinations from the stomach with fluoroscopic assistance showed no connection between the stomach and the esophagus.

Roentgenograms of the teeth revealed an abscess at the root of the upper left lateral incisor. This tooth was extracted later.

When we started the investigation, we hoped to obtain a complete mineral and nitrogen balance over a period of time during which no saliva entered the stomach and over a succeeding period during which saliva was added, for the purpose of comparison. We wished to do this before attempting dietary treatment. Dr. Jackson and his clinic group felt so confident of the necessity of saliva for growth

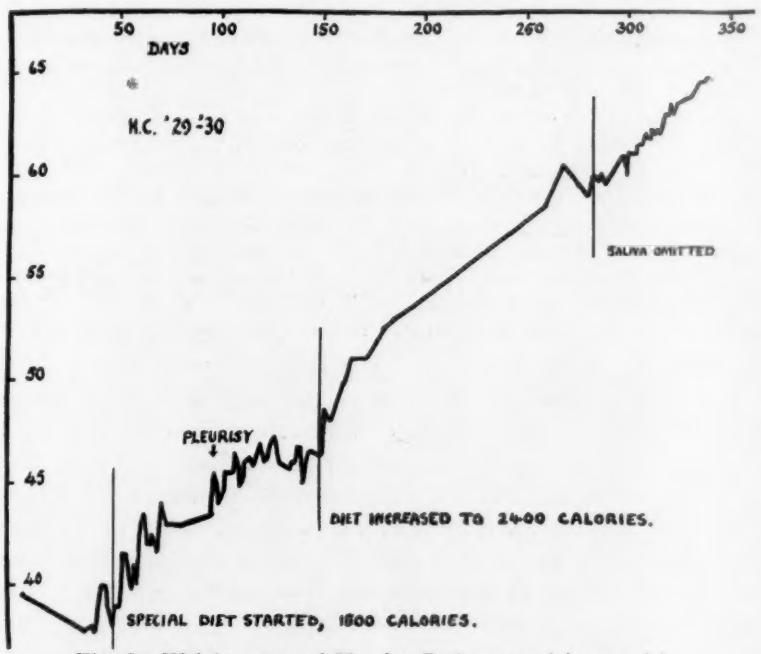

Fig. 2.—Weight curve of Harriet C. (expressed in pounds).

and were so disturbed over the patient's malnutrition that they felt it unwise to withhold saliva from the food, and the comparison of mineral and nitrogen balances at that time had to be abandoned. Later, at a time when the gain in weight was proceeding quite rapidly, observations of the chloride and nitrogen balances were made over a four day period, and the analyses showed positive balances, as expected.

On admission to the hospital, the patient had been instructed to chew all her food, to expel the food mixed with saliva into a bowl and to inject the mixture from the bowl into the fistula tube by means of a syringe. There were several factors that seemed to account for her failure to gain weight.

1. The constituents of the diet were not well balanced. Food, such as meat, toast and vegetables, were offered regularly, which required considerable mastication, and which, even then, could not pass through the fistula tube.

2. The caloric value of the food was not sufficient, owing in part to the amount that the tube excluded.

3. Between meals the patient was stealing candy, chewing gum and food, requiring large quantities of saliva, which was continually expectorated. The quantity of fluid lost in this way could not be estimated accurately.

In view of the immediate necessity of improving the patient's nutrition, our first step was to correct the diet. The food selected for her was made up into a fluid mixture of two liters containing the following: milk, 1,500 cc.; cream, 20 per cent, or 225 cc.; raw eggs, 6; Karo, 120 cc.; wheatena (uncooked), 30 Gm.; potato puree, 150 cc.; creamed soup, 250 cc.; apple sauce, 120 Gm.; bananas, 2; orange juice, 60 cc. (caloric value, 1,800).

Gradually we were able to prevent her from losing in expectoration large quantities of saliva by depriving her of chewing gum and food between meals.

Her anemia had practically disappeared previous to this dietary change, owing to the addition of iron to her diet, the red blood cells increasing from 2,470,000 to 4,300,000 in six weeks.

The immediate result of the change in diet was an astonishing increase in weight, as shown in figure 2. A second increase in the diet resulted in an even greater rapidity of gain (fig. 2).

In consideration of such a marked increase of weight, we felt justified in stopping the addition of saliva to the food. From March 25, 1930, the food was injected directly into the stomach without first entering the mouth. Despite the complete absence of saliva from the food, the weight gain continued at the same rate, as is obvious from figure 2. We consider this strong evidence against the hypothesis that a complete lack of saliva in the stomach markedly impedes growth.

Our experimental investigation of this hypothesis was carried out on fourteen young pigs, thirteen of which were from two litters. This work was reported in detail in another publication.[9]

In our animals of the first litter operated on under the supervision of Dr. I. S. Ravdin, the esophagus was freed and brought to the surface in the lateral line of the neck just posterior to the sternocleidomastoid muscle and allowed to heal with the skin sutured beneath it. Later it was divided. The two ends retracting thus formed fistulas, through the upper end of which saliva escaped, while through the lower end liquid food was given by tube. Certain animals were kept as controls and were given the same amounts of food as the animals operated on. The food was calculated according to weight. No additional water was given at first to take the place of that lost as saliva by the animals operated on. The difficulties of such a surgical procedure, which exposed the superior mediastinum, accounted for two deaths from infection. Two animals, one a control, died of porcine scabies, a particularly virulent disease among swine, and not at first recognized by us on account of its unusual appearance. Another animal on which operation was performed died of abscess of the lung, probably secondary to aspiration. The four remaining pigs, of which one was a control,

9. Wilder, T. S., and Stokes, J., Jr.: Esophageal Fistula in the Experimental Animal, Arch. Surg. **23**:111 (July) 1931.

gained weight consistently and were finally slaughtered on the one hundred and thirty-second day following operation.

In a second litter of five pigs of the same age as the previous group (one month), the same operation was performed on two, while the remaining three were left as controls. The weight curves of the animals operated on again compared favorably with those of the control pigs. None of this litter died. The animals operated on received an extra quantity of saline solution, differing only in this respect from the previous litter studied.

SUMMARY AND CONCLUSIONS

We have studied the effect of complete closure of the esophagus with the loss of saliva on the life and growth of a child of 10 years. Such closure appears to have no serious effect provided a well balanced diet is supplied. The addition of saliva and other secretions of the mouth to the food is probably unnecessary for the maintenance of a state of nutrition at least approaching normal.

Experimentally, we produced esophageal fistula by means of a three stage operation on young pigs. This work, reported elsewhere,[9] furnished evidence that growth will proceed at a rapid rate in this particular animal despite a complete loss of saliva.

MIGRATORY PERITONITIS

A CLINICOPATHOLOGIC STUDY OF SO-CALLED HEMATOGENOUS PERITONITIS IN CHILDREN *

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AND
O. SAPHIR, M.D.
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The question of the existence of a so-called primary or hematogenous form of peritonitis has long been debated. Up to the present time, no definite conclusions have been reached. During the past year several children were admitted to the Sarah Morris Hospital who subsequently came to autopsy with the clinical diagnosis of hematogenous peritonitis. In every case the postmortem examination revealed a definite origin for the inflammation of the peritoneum within the peritoneal cavity. In reality, the peritonitis was secondary to such a focus. The discrepancy in each of these cases between the clinical concept of the origin of the peritonitis and the true origin as revealed by the autopsy prompted us to a study of this form of peritonitis.

The work presented in this paper was undertaken, first, with the view of clarifying our own ideas as to what is meant by the terms "primary" and "hematogenous peritonitis" as used in the literature, secondly, to collect the existing evidence on which the concept of this form of peritonitis is based, and thirdly, to study a series of cases that were clinically diagnosed as hematogenous peritonitis. A detailed clinicopathologic study seemed to be the only method of obtaining data sufficiently accurate to justify any conclusions as to the existence or nonexistence of a primary or hematogenous form of peritonitis.

LITERATURE

Literature on this subject is not lacking but is most confusing. Many observers believe that primary or hematogenous peritonitis not only occurs but may even be manifested in epidemic forms. Other investigators, however, have called attention to its extreme rarity and have gone so far as to doubt or completely deny its existence.

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* From the Sarah Morris Children's Hospital and the Department of Pathology of Michael Reese Hospital.

* Aided by the Otto Baer Fund for Clinical Research.

The historical details of this interesting controversy have been amply reviewed. It will therefore be sufficient to mention that as early as 1864, Behier and Hardy [1] described a form of peritonitis that they considered hematogenous in origin. Since that time many contributions have been published, and the present literature comprises a mass of material.

A review of this literature reveals much confusion in the concept of hematogenous peritonitis and a lack of uniformity in nomenclature. Even the more recent publications have designated by various names the form of peritonitis that supposedly occurs without a demonstrable focus within the peritoneal cavity. DeSanctis and Nichols [2] spoke of

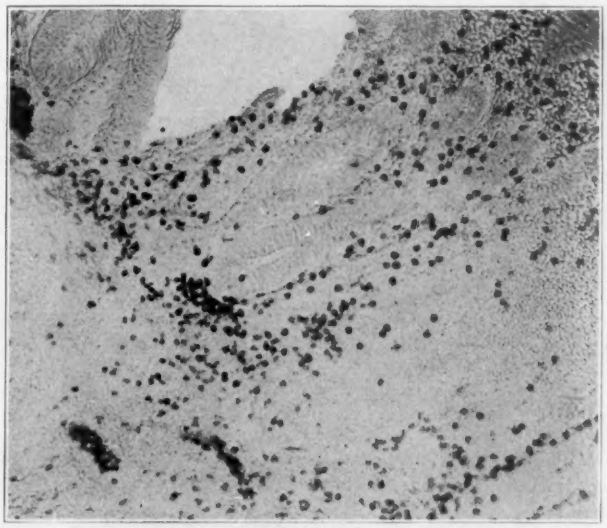

Fig. 1.—Mucosa and submucosa of the intestines (oxydase reaction). Note the conspicuous appearance of the polymorphonuclear leukocytes; × 180.

"primary peritonitis" and Koch [3] of "idiopathic peritonitis"; Rabinowitz [4] used the term "hematogenous peritonitis"; Girgensohn preferred "metastatic peritonitis"; Wolff [5] suggested the term "cryptogenic peri-

1. Behier, L., and Hardy, A., quoted by Hertzler, A. E.: The Peritoneum, St. Louis, C. V. Mosby Company, 1921.

2. DeSanctis, A. G., and Nichols, R. A.: Primary Peritonitis in Children, Arch. Pediat. **46**:17, 1929.

3. Koch, K.: Zur Aetiologie der akuten serösen "idiopathischen" Peritonitis, Zentralbl. f. Chir. **52**:1240, 1925.

4. Rabinowitz, M. A.: Acute Hematogenous Streptococcic Peritonitis, Am. J. M. Sc. **157**:797, 1919.

5. Wolff, H.: Kryptogene Peritonitis und Menstruation, Deutsche med. Wchnschr. **55**:1174, 1929.

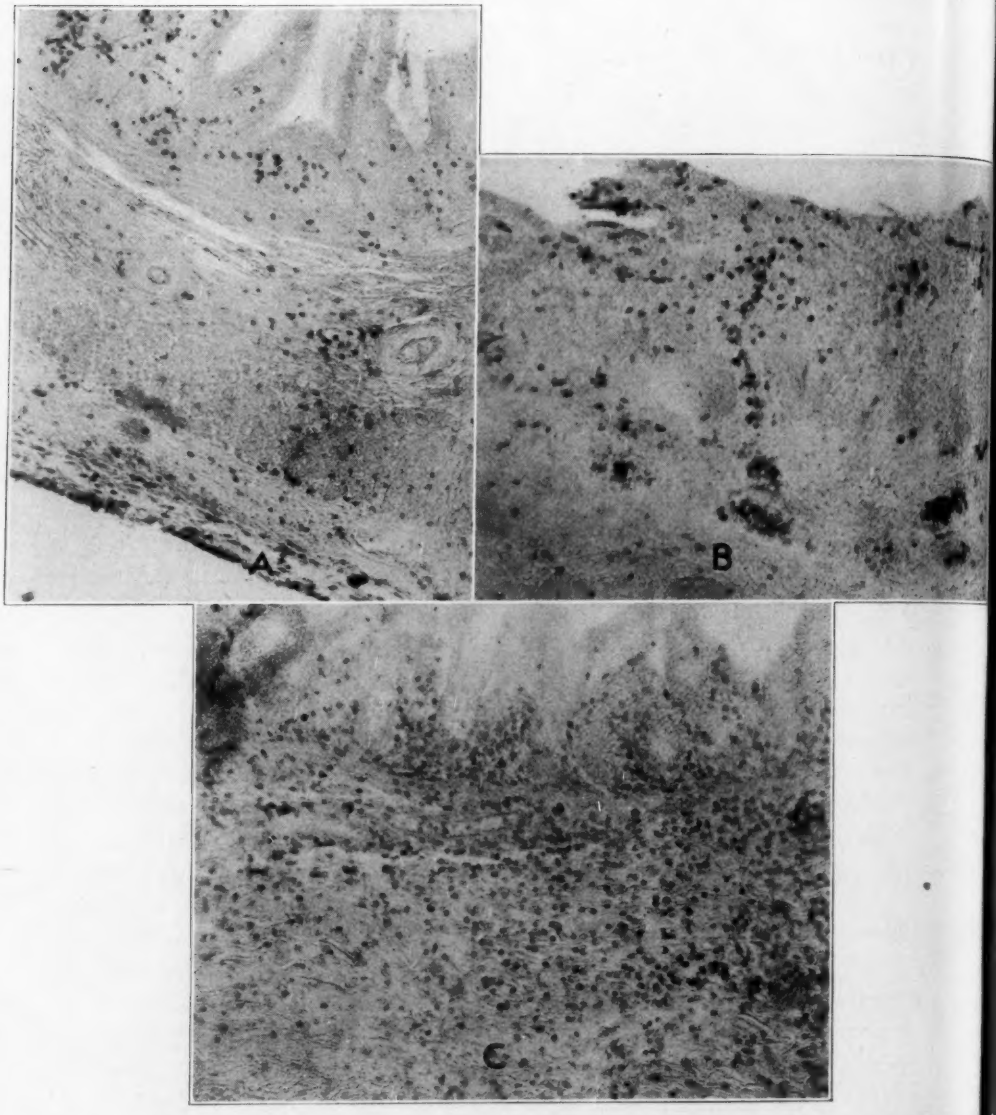

Fig. 2.—A section of the small intestine (oxydase reaction). Note the presence of polymorphonuclear leukocytes in the muscular coats. *A*, × 120; *B*, × 120; *C*, × 140.

tonitis"; Schopf [6] spoke of "infants' peritonitis," and Melchior's [7] "peritonitis serosa acuta" probably also belongs to this group. Still other writers prefer terms indicating the causative organisms. McCartney and Fraser [8] spoke of "pneumococcic peritonitis" and Ruppanner [9] of "streptococcic peritonitis."

By some authors these terms are used interchangeably. Others employ "hematogenous" or "metastatic peritonitis" only for those cases in which the micro-organisms from some distant focus are thought to have reached the peritoneal cavity by way of the blood stream. Having reached the peritoneal cavity, the micro-organisms supposedly set up

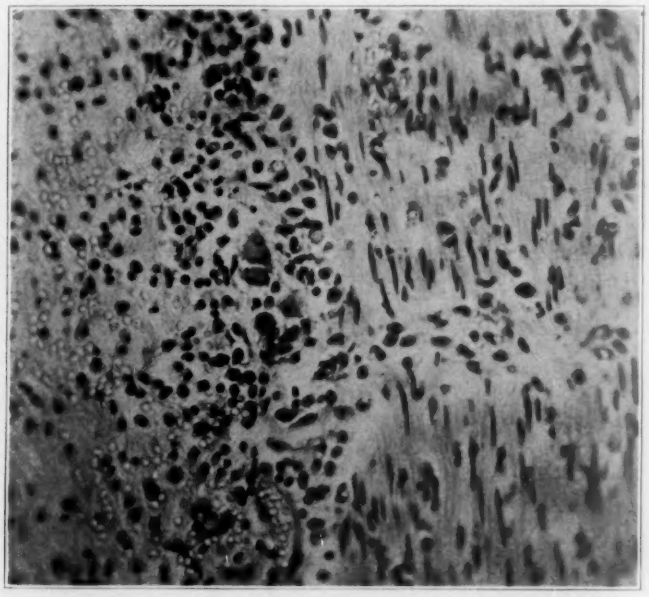

Fig. 3.—A section of the submucosa and muscularis of the small intestine. Note the inflammatory cells in the submucosa and the slight involvement of the muscularis. Iron-hematoxylin-eosin stain; × 260.

a diffuse inflammation without first producing a demonstrable local lesion. A preexisting bacteremia is, of course, assumed. These authors reserve the terms "primary," "idiopathic" or "cryptogenic peritonitis" for those cases in which even a remote primary focus could not be

6. von Schopf, E. M.: Ueber Säuglingsperitonitis, Ztschr. f. Kinderh. **44**:100, 1927.

7. Melchior, E.: Zur Beurteilung der Peritonitis serosa acuta (idiopathica?), Zentralbl. f. Chir. **51**:2792, 1924.

8. McCartney, J. E., and Fraser, J.: Pneumococcal Peritonitis, Brit. J. Surg. **9**:479, 1922.

9. Ruppanner, E.: Ueber metastatische Streptokokken Peritonitis, Schweiz. med. Wchnschr. **52**:610, 1922.

demonstrated. The term "primary peritonitis," implying an idiopathic or hematogenous form of the disease, is especially confusing because, according to Kaufmann [10] and to Gierke,[11] the term "primary peritonitis" is applied to those cases in which the micro-organisms reached the peritoneal cavity directly by means of a perforating trauma or following an operative procedure.

While most clinicians believe in the occurrence of hematogenous peritonitis, its existence is not generally accepted by the pathologist. This is due to the fact that the postmortem examination often discloses starting points for the peritonitis within the peritoneal cavity in cases in which the clinician, because of the absence of clinical findings indicating a preceding abdominal lesion, has considered the peritonitis to be hematogenous in origin.

As opposed to the conception of hematogenous peritonitis that necessitates the assumption of a remote focus of infection and a subsequent bacteremia, the cause of peritonitis is often found within the peritoneal cavity. According to Kaufmann,[10] peritonitis may be caused by perforation of one of the organs in the peritoneal cavity, by direct extension of an inflammatory process from an organ covered by peritoneum or by invasion of the peritoneal cavity by bacteria from adjacent structures without perforation. This last type of peritonitis is referred to in the German literature as "Durchwanderungs-Peritonitis." Reference to this form will be made in greater detail later in this paper.

MATERIAL

This study deals with twenty-four cases of peritonitis in children. Even though various possible extra-abdominal sources for the peritonitis presented themselves clinically, the actual cause of the peritonitis in each case was disclosed at postmortem examination only by complete gross and histologic examination of the organs within the peritoneal cavity.

REPORT OF CASES

CASE 1.—A girl, aged 7 months, had had a cold two weeks prior to entering the hospital. Five days before admission, a high fever developed, and the child became restless and irritable and began to vomit. These symptoms persisted on admission. Examination revealed an extremely toxic infant with a temperature of 102 F. There was a suppurative otitis media on the right side. The abdomen was soft. The white cell count was 18,600. The clinical diagnosis was septicemia. The vomiting continued, and the following day the abdomen was markedly distended and tender.

10. Kaufmann, E.: Lehrbuch der speziellen pathologische Anatomie, ed. 7 and 8, Berlin, G. Reimer, 1922.

11. von Gierke, E.: Bauchfell, in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 6.

A diagnosis of hematogenous peritonitis was made, and the child was operated on. At operation no intra-abdominal focus of the peritonitis could be demonstrated. The child died twelve hours later.

Autopsy revealed acute catarrhal enteritis and acute fibrinopurulent peritonitis. Cultures taken from the heart's blood, from the peritoneal exudate, from the mucosa in the region of the enteritis and from the intestinal contents revealed the same type of streptococci (Streptococcus hemolyticus). The peritonitis can be explained as secondary to the enteritis.

CASE 2.—A girl, 10 years old, became ill with headache, chills and fever two days before admission to the hospital. The following day she vomited several times and had two convulsions. There had been from three to five bowel movements daily. The fever and vomiting persisted on admission. Examination revealed an acutely ill child with a temperature of 102 F. The pharynx was reddened. The abdomen was distended and tender. The clinical diagnosis was acute peritonitis. An exploratory operation was performed. The appendix was normal. No primary focus of peritonitis was found within the peritoneal cavity, and the peritonitis was considered to be hematogenous in origin. The child died two days after admission.

At autopsy, there were found acute purulent peritonitis, acute catarrhal enteritis and cholecystitis. Pneumococci were recovered from the ileum, gallbladder and peritoneum. Pathologically, the case may be explained on the basis of a primary enteritis and cholecystitis, with secondary peritonitis.

CASE 3.—A 7 weeks old boy was admitted to the hospital because of diarrhea and vomiting of several days' duration. He had had a cold a few days prior to admission. On examination, the infant appeared extremely toxic. The temperature was 102 F. The throat and pharynx showed no changes. The abdomen was distended. The white cell count was 28,000. The clinical diagnosis was acute hematogenous peritonitis, probably secondary to an infection of the upper respiratory tract. The child died five days after admission.

Autopsy revealed acute fibrinous peritonitis, acute catarrhal ileocolitis, bronchopneumonia and acute fibrinous pleuritis. The peritonitis could be explained as secondary to the acute catarrhal ileocolitis.

CASE 4.—A boy, 4 months old, became ill with high fever forty-eight hours before entering the hospital. The day before admission, he had several convulsions and diarrhea and vomiting developed. Examination revealed a moribund infant with a temperature of 106 F. The abdomen was soft. The child vomited shortly after admission and expired six hours later. The clinical diagnosis was septicemia with secondary peritonitis.

At autopsy there were found acute fibrinopurulent peritonitis, acute catarrhal ileocolitis and acute mesenteric lymphadenitis. Smears taken from the peritoneal exudate showed many gram-positive cocci in chains. The ileocolitis seemed to be the most probable source of the peritonitis.

CASE 5.—A boy, 8½ months old, had a history of coughing for a period of several weeks. The present illness began one week before admission to the hospital with fever followed by convulsions. The child had been vomiting since the day before admission. Examination revealed a toxic infant with a temperature of 106 F. and a respiratory rate of 56 per minute. The pharynx was red. There was impaired resonance over the lower lobe of the right lung, with bronchial breathing over this area. The abdomen was distended and rigid. The white cell count was 24,000. The clinical diagnosis was pneumonia and hematogenous peritonitis. The child died two days after admission.

Autopsy showed acute fibrinopurulent peritonitis and acute and subacute catarrhal enteritis. Bilateral bronchopneumonia with bilateral acute fibrinopurulent pleuritis was also present. The peritonitis was explained on the basis of the enteritis. Cultures of the peritoneal cavity and of the heart's blood showed hemolytic streptococci.

CASE 6.—A boy, 5½ months of age, had a history of fever, sweats and cough for five days prior to admission to the hospital. Examination revealed an acutely ill infant with a temperature of 103 F. and a respiratory rate of 78 per minute. The pharynx was red. The right lung showed clinical evidence of bronchopneumonia. The abdomen was distended and rigid. The white cell count was 2,400. The clinical diagnosis was pneumonia and hematogenous peritonitis. The child died twenty-four hours after admission.

Autopsy showed acute seropurulent peritonitis, acute ulcerative enteritis and pneumonia involving the right lung. Cultures of the blood and of the peritoneal exudate showed nonhemolytic streptococci. The source of the peritonitis was thought to be the acute ulcerative enteritis.

CASE 7.—A girl, 18 days old, developed red spots on the body four days before admission to the hospital. Twenty-four hours later, a swelling of the ankles and labia was noted. The infant was drowsy and irritable. Clinically, the child appeared acutely ill. The abdomen was markedly distended. The labia were red and swollen. The umbilicus appeared normal. The clinical diagnosis was septicemia and hematogenous peritonitis. The child died eight hours after admission.

At autopsy there were found acute seropurulent peritonitis, acute periomphalitis, acute suppurative thrombophlebitis of the umbilical vein and acute purulent pylephlebitis. Cultures from the peritoneal surface yielded a pure growth of hemolytic streptococci. The cultures from the heart remained sterile. The source of the peritonitis was thought to be the acute pylephlebitis and the thrombophlebitis of the umbilical vein.

CASE 8.—A boy, 6 weeks old, developed fever five days before admission. Twenty-four hours later, swelling and redness of the scrotum were noted. He had had several convulsions. Examination revealed an extremely irritable infant. The temperature was 102 F. The abdomen was distended. The liver and spleen were palpable. There was phimosis, with swelling, redness and induration of the scrotum and the lower abdominal wall. The white cell count was 12,500. The clinical diagnosis was phimosis, cellulitis of the perineum and lower abdominal wall, with septicemia and possible peritonitis. The child died twelve hours after admission.

Autopsy revealed acute serofibrinous peritonitis and a phlegmonous inflammation of the anterior abdominal wall, the perineum and the scrotum. Pus was found extending into the abdominal muscles. The source of the peritonitis in this case was the phlegmonous inflammation of the abdominal wall. It could not be determined whether or not this inflammation was the result of a primary umbilical infection.

CASE 9.—A boy, 3 months of age, entered the hospital because of a cold and slight fever of several days' duration. Examination revealed an emaciated infant with marked snuffles. There was a brownish macular rash over the body. The temperature was 100.2 F. The pharynx was reddened, and the spleen and liver were palpable. There was a bilateral hydrocele. The white cell count was 32,000. The clinical diagnosis at that time was congenital syphilis, bilateral hydrocele and

acute pharyngitis. Two days after admission to the hospital, the temperature reached 102 F., the abdomen became tense and distended, and the child vomited frequently. There were many râles over the upper lobe of the right lung. The diagnosis was bronchopneumonia and probable hematogenous peritonitis. The child died three days after admission.

Autopsy revealed acute diffuse fibrinopurulent peritonitis, subacute perinephritic abscess, subacute pyelitis and acute peri-orchitis. The source of the peritonitis in this case apparently was the perinephritic abscess.

Case 10.—A girl, 6 years old, developed malaise and fever eight days before admission to the hospital. Two days later, she complained of intermittent abdominal pain which had gradually become more severe. At the time of admission, the child also complained of headaches. On examination she appeared acutely ill. The temperature was 105 F. and the pulse rate 132. The pharynx was red. There was cervical adenitis. The abdomen was distended, rigid and tender. The white cell count was 7,000. The Widal test gave negative results. The clinical diagnosis was acute pharyngitis, cervical adenitis and acute hematogenous peritonitis. In view of the abdominal findings, an exploratory operation was deemed advisable. At the operation, generalized peritonitis was disclosed, but no focus of peritonitis was found within the abdominal cavity. The patient died four days after operation.

Autopsy showed acute fiibrinopurulent peritonitis. There was a marked hyperplasia of Peyer's patches, which on histologic examination proved to be the seat of medullary swelling of typhoid. The blood cultures showed B. typhosus. The source of the peritonitis in this case was apparently the typhoid enteritis.

Case 11.—A girl, 3½ months old, had had a cold for two weeks. Four days prior to admission to the hospital fever developed and forty-eight hours later the abdomen became distended. Examination revealed an acutely ill infant with a temperature of 104 F. The abdomen was distended and rigid. The white cell count was 11,900. The clinical diagnosis was hematogenous peritonitis. The child was operated on, and no focus of peritonitis was found within the peritoneal cavity. She died two days later.

Autopsy revealed acute fibrinopurulent peritonitis. There were multiple tumors of the liver, apparently congenital hepatomas, advanced bilateral bronchopneumonia and empyema on the left side. The source of the peritonitis in this case was the empyema.

Case 12.—A girl, 6 months of age, had had a cough, running from the nose and fever for five days prior to admission. Two days before entering the hospital, she had had several convulsions. Examination revealed an extremely toxic infant with a temperature of 106 F. The throat was red. There were impaired resonance and a prolonged expiratory phase over the middle and lower lobes of the right lung. The abdomen was distended, and there was dulness in both flanks. The white cell count was 9,900. The clinical diagnosis was pneumonia and hematogenous peritonitis. The child died twenty-four hours after admission.

At autopsy, fibrinopurulent peritonitis, bronchopneumonia with empyema and acute pyelitis were found. Cultures of the heart's blood showed hemolytic streptococci, while cultures of the peritoneal exudate revealed nonhemolytic streptococci. The source of the peritonitis in this case was the empyema.

Case 13.—A boy, 3 weeks old, had had swelling of the scrotum for one week. Two days before admission to the hospital, the infant began to vomit; during this period he had been markedly constipated. Examination revealed an emaciated infant with a temperature of 102 F. The pharynx was injected. The abdomen was

distended and tense. There was a mass in the right inguinal canal and the scrotum, which was reduced during the examination. The white cell count was 21,000. The clinical impression was that the condition was incarcerated hernia, intestinal obstruction and peritonitis. An exploratory laparotomy was performed, and acute peritonitis was found. There was no incarcerated hernia, and the intestines appeared to be normal. Because no demonstrable focus could be found at operation, the peritonitis was considered to be hematogenous in origin. The child expired twenty-four hours later.

At autopsy, diffuse fibrinopurulent peritonitis and acute catarrhal enteritis were found. The cultures from the heart's blood revealed hemolytic streptococci, while the cultures from the peritoneum showed nonhemolytic streptococci. The peritonitis was explained by the catarrhal enteritis.

Case 14.—A 5 weeks old boy had had an infection of the foot for three weeks prior to admission. This had gradually grown worse, and the foot had become red and swollen. Five days before entering the hospital, the child became irritable and had a slight elevation of temperature. Examination revealed a phlegmonous inflammation of the right foot. The abdomen was tense. The umbilicus appeared normal. There was otitis media on the right side. The temperature on admission was 101.4 F. The clinical diagnosis was phlegmonous inflammation of the right foot and otitis media. Eighteen days after admission, the abdomen became distended and the child started to vomit. The clinical diagnosis at that time was acute peritonitis, probably hematogenous in origin. The child died twenty-four hours later.

Autopsy revealed acute fibrinopurulent peritonitis and thrombophlebitis of the umbilical vein. There were otitis media and acute mastoiditis. Cultures from the peritoneum showed nonhemolytic streptococci, while the heart's blood remained sterile. The source of the peritonitis was the omphalothrombophlebitis.

Case 15.—A girl, 4½ years of age, had had a tonsillectomy three weeks before admission. Four days before entering the hospital, she had had an intermittent fever associated with constipation and frequent vomiting. On examination, the child appeared acutely ill. The temperature was 107 F. The lips were cyanotic. The throat was normal and the abdomen soft. The white cell count was 16,000. The clinical diagnosis was septicemia and peritonitis. The child died eight hours after admission.

Autopsy revealed acute fibrinopurulent peritonitis and acute ulcerative enterocolitis. Smears from the peritoneum showed streptococci, and smears from the intestinal mucosa also showed streptococci and gram-negative bacilli. The source of the peritonitis was the acute ulcerative enterocolitis.

Case 16.—A 3 months old boy became ill three days prior to admission, with fever and vomiting. During this period, there had been a slight loss in weight. Examination revealed a reddened pharynx and otitis media on the left side. The temperature was 103.6 F. The white cell count was 2,000. The clinical diagnosis was acute pharyngitis and otitis media. The vomiting and fever continued, and three days after admission the abdomen became distended and tender. The clinical diagnosis was then metastatic peritonitis. An exploratory laparotomy was performed. Peritonitis was found, but no primary focus was demonstrable within the peritoneal cavity. The child died two days after operation.

At the autopsy, acute fibrinopurulent peritonitis acute and subacute enterocolitis, bronchopneumonia and acute fibrinous pleuritis were found. The source of the peritonitis was the enterocolitis.

Case 17.—A 3 weeks old boy entered the hospital with a history of diarrhea of four days' duration. Fever, vomiting and drowsiness had been present for forty-

eight hours prior to admission. Examination revealed an acutely ill, drowsy infant. The throat was red. The abdomen was distended and rigid. The clinical diagnosis was septicemia and peritonitis. The child died twenty-four hours after admission.

Autopsy revealed acute fibrinopurulent peritonitis and acute catarrhal enteritis. The source of the peritonitis was the enteritis.

CASE 18.—A girl, 2 years and 7 months old, developed fever, vomiting and abdominal pains twelve hours before admission. On examination the child appeared quite toxic. The temperature was 101.2 F. The throat was reddened. There was generalized rigidity and tenderness of the abdomen. The white cell count was 15,000. The clinical diagnosis was hematogenous peritonitis. An exploratory laparotomy was performed. No focus that could have explained the peritonitis was found in the peritoneal cavity at operation. The child died twelve hours after admission.

At autopsy, there were found acute purulent peritonitis and acute and subacute enteritis. Type 4 pneumococcus was isolated from the peritoneum. The source of the peritonitis was the acute and subacute enteritis.

CASE 19.—A boy, 27 months of age, had a cold two weeks prior to admission. Four days before entering the hospital, diarrhea developed. The cold had become worse, and the child had complained of abdominal pain. Examination revealed an acutely ill infant with a temperature of 102.8 F. The abdomen was distended and tender. The white cell count was 13,800. The clinical diagnosis was acute peritonitis. An exploratory laparotomy was performed, but no focus to explain the peritonitis was found within the peritoneal cavity. The peritonitis, therefore, was considered to be hematogenous in origin. The child died four days after operation.

Autopsy revealed generalized fibrinopurulent peritonitis and acute ulcerating enteritis. The source of the peritonitis in this case was the enteritis.

CASE 20.—A girl, 2 years old, was admitted to the hospital because of refusal to nurse and because of continuous moaning and increasing drowsiness. Examination revealed an apathetic, irritable infant with a temperature of 99.2 F. The mucosa of the mouth was reddened. The skin was excoriated. The abdomen was distended. The liver was palpable. The white cell count was 2,600. The clinical diagnosis on admission was acute infection of the upper respiratory tract. The child began to vomit shortly after admission, and the abdomen became more distended and rigid. The clinical impression at that time was sepsis and peritonitis. The child died forty-eight hours after admission.

Autopsy showed acute fibrinopurulent peritonitis and thrombophlebitis of the umbilical and portal vein. The source of the peritonitis was thought to be the thrombophlebitis of the umbilical and portal veins.

CASE 21.—A boy, 7 months of age, had been restless and irritable and had had intermittent fever for two weeks. Twelve hours prior to admission, diarrhea developed and the child vomited once. Examination revealed an extremely toxic infant with a temperature of 103 F. The pharynx was markedly injected and edematous, and the cervical glands were enlarged. The abdomen was rigid and apparently tender. The white cell count was 56,000. The clinical diagnosis was acute pharyngitis and hematogenous peritonitis. The child was operated on, and no source of the peritonitis was found in the peritoneal cavity.

At autopsy, acute purulent peritonitis and acute catarrhal enteritis were observed to be present. Postmortem cultures of the heart's blood and of the peritoneal exudate revealed hemolytic streptococci. Pathologically, the peritonitis could be explained on the basis of a primary enteritis.

CASE 22.—A boy, 4 weeks old, had had jaundice since birth. Two weeks before admission, there had been severe bleeding after a circumcision. Examination revealed a small infant with moderate generalized icterus. The face was of the mongolian type. The abdomen was distended and tympanitic. The white cell count was 8,600. The clinical diagnosis was mongolian idiocy and icterus neonatorum. Fourteen days after admission diarrhea developed and the child began to vomit. The diarrhea and vomiting became progressively worse. The child steadily became weaker and died four weeks after admission.

The autopsy showed acute fibrinopurulent peritonitis and acute and subacute enteritis. The source of the peritonitis was the acute and subacute enteritis.

CASE 23.—A girl, 3½ years of age, had had diarrhea and fever for four days prior to admission. Blood and mucus had been noted in the stools. Clinically, the child appeared acutely ill. The mucosa of the throat was hyperemic, and the tonsils were enlarged and red. The temperature was 102.2 F. Clinical signs of pneumonia were present over the right lung. There was a generalized tenderness of the abdomen. The white cell count was 18,000. The clinical diagnosis was enteritis and bronchopneumonia. The child died twenty-four hours after admission.

Autopsy showed acute fibrinopurulent peritonitis and acute and subacute diffuse ulcerative enterocolitis. Cultures of the feces revealed the presence of B. dysenteriae.

CASE 24.—A girl, 6 months of age, had a temperature of 102 F. five days prior to admission. There was apparent pain and difficulty on urination. On examination the child did not appear to be acutely ill. The temperature was 102 F. The mucosa of the pharynx was reddened. The urine contained a large quantity of pus. The white cell count was 15,000. The clinical diagnosis was acute pharyngitis and acute pyelitis. The fever and pyuria persisted. Twelve days after admission signs of bronchopneumonia appeared. Two weeks later, cellulitis of the neck developed. The child died one month after admission.

Autopsy revealed acute fibrinopurulent peritonitis, bilateral pyelonephritis and thrombophlebitis of the left renal vein. There was bilateral otitis media, with bilateral mastoiditis and also bilateral bronchopneumonia with fibrinopurulent pleuritis. The source of the peritonitis in this case was the thrombophlebitis of the left renal vein.

CLINICAL COMMENT

Twenty-one of our twenty-four cases were diagnosed clinically as hematogenous peritonitis. All the patients were children, the ages ranging from 18 days to 10 years. Twelve were boys and nine were girls. In every instance, a distant focus of infection could be demonstrated which clinically was considered to be the source of the peritonitis. In twelve cases there was either the clinical evidence of an acute pharyngitis or tonsillitis or the history of a recent infection of the upper respiratory tract. Four other cases showed additional findings of bronchopneumonia. In three cases the peritonitis was thought to be secondary to septicemia, the original focus of which could not be determined. In the remaining two cases, cellulitis of the foot and an infection of the abdominal wall were respectively considered to be the primary focus that had led to the peritonitis. Nine exploratory laparot-

omies were performed in this group of patients. At the operations, no source of the peritonitis could be demonstrated within the peritoneal cavity. In three patients of our series there had been no clinical manifestation of the peritonitis that was disclosed at the postmortem examination. These cases are included merely as additional examples of the lesion in question.

The history, as a rule, was that from three to four days prior to admission to the hospital, the patient had suddenly become ill with a high fever accompanied by constitutional symptoms, nervous disturbances and prostration. Vomiting was often an early symptom, though it was not present in all cases. Diarrhea occurred in only eight instances. The abdomen was generally tender and often distended. The white blood cell count was inconstant, varying between 2,000 and 50,000, though leukocytosis was found in most instances. All the patients appeared to be acutely ill from the time they were first seen; they rapidly passed into the terminal stage of acute peritonitis, and died from two to ten days after the onset of the illness. From an analysis of these cases we were unable to draw any conclusions in regard to a definite clinical syndrome of diagnostic value.

PATHOLOGIC COMMENT

Sixteen of our twenty-four cases showed evidence of intestinal lesions. Of these, six presented acute catarrhal enterocolitis, four acute and subacute enterocolitis and four acute ulcerative enterocolitis. One case revealed typhoid enteritis and another dysenteric enteritis. In two of these cases a clinical diagnosis of peritonitis was not made. Three of the twenty-four cases showed thrombophlebitis of the umbilical veins and one case thrombophlebitis of one renal vein with acute bilateral pyelonephritis (the clinical diagnosis of peritonitis was not made in this case). An acute and subacute perinephritic abscess was present in one case and empyema in two cases; in another case there was a phlegmonous inflammation of the scrotum, perineum and abdominal muscles.

Cultures of the peritoneal exudate revealed the presence of streptococci in eight cases. In two of these cases, the blood cultures were negative. In two other cases, nonhemolytic streptococci were obtained from the peritoneal exudate and hemolytic streptococci from the blood. Three cases showed nonhemolytic streptococci in both the blood and the peritoneal exudate. In one case, hemolytic streptococci were cultured from the heart's blood, the peritoneal exudate, the mucosa of the intestines and the feces. In two of the cases that showed enteritis at postmortem examination, pneumococci were found in the peritoneal exudate, and in one of these cases similar organisms were also obtained

from the lumen of the small intestine. In another case, streptococci were observed in smears taken from the peritoneal exudate and from the intestinal mucosa. In one case, typhoid bacilli were obtained from the intestines, and in another case B. dysenteriae Shiga. All of these cultures were made at the time of autopsy.

Special attention was paid to the histologic changes in the gastrointestinal tract, and many sections were taken from the various portions. While some of the sixteen cases with intestinal lesions showed only slight enteritis on gross examination, histologically the changes were marked. It could be seen in the sections, especially in those taken from about the midportion of the ileum, that the inflammatory process had extended through the mucosa and submucosa. The continuity of the surface of the mucosa was repeatedly interrupted, and minute ulcers were present in many places. There was a marked infiltration of polymorphonuclear leukocytes throughout the mucosa and submucosa. Endothelial cells and lymphocytes were also present. Most of the peritoneal exudate seemed to be found in the regions corresponding to those portions of the intestines that showed the more severe lesions in the mucosa and submucosa. The muscular coats revealed no changes in sections stained with hematoxylin-eosin. In frozen sections, however, which were prepared with alpha-naphthol and dimethyl-p-phenylenediamine, a number of polymorphonuclear leukocytes were found in the muscular coats. Although these cells were not noted in hematoxylin-eosin preparations, the prominence of the granules as revealed by the oxydase reaction left no doubt as to their identity. In some of our cases, by the use of the Gram-Weigert stain, gram-positive cocci could be demonstrated not only in the mucosa, submucosa and peritoneal surface, but in the muscular coat. In the latter location, they were not found in vessels but apparently were free in the tissue and lymph spaces.

Sections of the small intestines of patients who died from peritonitis as a result of perforated appendixes or peptic ulcers were stained for bacteria with the Gram-Weigert stain and for polymorphonuclear leukocytes with the oxydase stain. These sections were taken from portions of the small intestines that showed a marked peritoneal exudate, but not from the regions of the perforations. This was done as a control to see whether the muscular coat, the mucosa and the submucosa of the intestines in these cases might also show leukocytic infiltration and bacteria similar to our cases of enteritis. While in some instances polymorphonuclear leukocytes were found in the outermost layers of the muscular coat directly extending from the peritoneal exudate, they were absent in the other coats of the intestines. In none of the sections could bacteria be demonstrated in the muscular coat. On the other hand, the changes in the muscular coat of the intestines in our cases

of enteritis were much less marked than changes in the muscular coat of appendixes showing suppurating inflammation in which the inflammatory exudate had extended massively through the muscular coat, reaching the peritoneal surface by direct extension (peritonitis per extensionem).

In our cases of enteritis, the involvement of the peritoneum from the adjacent intestinal wall in which evidence of inflammatory reaction and, in some cases, the presence of bacteria had been demonstrated seems to us a much more reasonable explanation of the peritonitis than the purely speculative hematogenous origin.

The peritonitis in the cases of omphalophlebitis, of thrombophlebitis of the renal vein and of perinephritis can also be explained by a similar invasion of the adjacent peritoneum by bacteria from these respective sites. The close proximity of these primarily diseased structures to the peritoneal cavity suggests a secondary involvement of the peritoneum. In the cases of phlebitis, the peritoneum might have been involved by direct extension of the inflammatory process from the wall of the vein or by invasion of the bacteria without actual extension of the inflammatory process. The latter mechanism may also have been the underlying explanation for the peritonitis in the case showing perinephritis. While such an explanation could not be conclusively proved in our cases, it seems to us most likely. The bacteria in the cases of peritonitis following empyema might have reached the peritoneum through the diaphragm. Burckhardt [12] and, more recently, von Gierke [11] have called attention to the fact that empyema may be the starting point of peritonitis. The empyema in our cases was the result of an organizing bronchopneumonia. In the diaphragm in both cases of empyema, polymorphonuclear leukocytes were demonstrated by the use of the oxydase stain. We have no definite proof that the diaphragm was involved primarily from its pleural surface, but the existence of the bronchopneumonia and the empyema, both of which were definitely of longer duration than the peritonitis, suggests that the peritonitis followed the empyema. The phlegmonous inflammation of the anterior abdominal wall in case 8 was the source of the peritonitis either by continuity of the inflammatory exudate or by an invasion of the surrounding tissue by bacteria, including the peritoneal cavity.

HEMATOGENOUS PERITONITIS

Clinically, twenty-one of our twenty-four cases of peritonitis were thought to be hematogenous in origin. It is interesting to analyze these cases from this point of view, and see what evidence can be summoned to justify such a diagnosis.

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12. Burckhardt, E.: Ueber Kontinuitätsinfektion durch das Zwerchfell bei entzündlichen Prozessen der Pleura, Beitr. z. klin. Chir. **30**:731, 1901.

In nine of the twenty-one cases the patients were operated on. At the operations and subsequent histologic examinations, none of the appendixes that were removed revealed any abnormalities. Furthermore, a thorough examination of the abdominal organs at the time of operation did not disclose a source of the peritonitis within the peritoneal cavity. After primary inflammation of one of the peritoneal viscera was eliminated as a cause, the peritonitis was considered hematogenous in origin. The latter diagnosis seemed all the more plausible, because in each of the nine cases there was either the clinical evidence or the history of a recent infection of the respiratory tract. In the remaining twelve cases a careful history and thorough clinical examination seemingly ruled out the possibility of the existence of a primary inflammatory process in the peritoneal cavity but did reveal the presence of various inflammatory foci remote from the peritoneum. In three cases the clinical concept as to the hematogenous origin of the peritonitis was apparently confirmed by the finding of the same type of organism in both the blood cultures and cultures taken from the peritoneal exudate.

The literature that we have reviewed would lead us to believe that hematogenous peritonitis not only exists, but seems to be of relatively frequent occurrence. The conception on which this belief is based may be summarized as follows: Histories, clinical examinations and laparotomies seem to indicate the absence of a primary focus within the peritoneal cavity in a certain number of cases of peritonitis but, at the same time, suggest a primary remote focus such as an infection of the upper respiratory tract, inflammations of the lung and pleura or septicemia, the portal of entry of which may or may not be obscure. A small number of cases are reported in which even a postmortem examination revealed no primary lesion within the peritoneal cavity which was considered to be the origin of the peritonitis. In a number of cases the same type of organism was obtained from cultures of the blood and of the peritoneal exudate.

It may be seen that the evidence for the existence of a hematogenous form of peritonitis is almost entirely negative in character, being largely dependent on the absence of positive findings. As such, it can carry but little weight when opposed to positive evidence favoring a different etiology of the peritonitis in the same group of cases. While, clinically, none of our cases showed a lesion within the peritoneal cavity severe enough to be held responsible as a possible source of the peritonitis, even after exploratory laparotomy in nine of the twenty-four cases, autopsy did reveal such a lesion in every case, either in the peritoneal cavity or in structures adjacent to the peritoneum.

It is true that sixteen of our cases of peritonitis gave clinical evidence or a history of a recent infection of the respiratory tract. It

remains, however, to be proved that there was an actual relation between the infection and the peritonitis. Thirteen hundred and nine children admitted to the Sarah Morris Hospital over the same period of time in which the cases of peritonitis that are reported occurred, presented the physical findings of an acute infection of the respiratory tract. None of these children presented any evidence of peritoneal involvement. We refer to this statement only for statistical purposes, but we should like to draw attention to the fact that only 1.2 per cent of children with infections of the respiratory tract showed peritonitis.

Furthermore, it is difficult to understand why the peritoneum, which is known to be so resistant to invasive organisms, should be the single place of manifestation of a blood-borne infection starting from a distant primary focus. The bone marrow is known to be a favored localization for an infection of the blood stream because of the peculiar arrangement of the blood vessels in the region of the epiphyses. As a matter of fact, osteomyelitis is the most common among blood-borne infections in childhood. None of our cases, however, showed any of the more common secondary manifestations of bacteremia. If we believed that a special strain of bacteria exists that has a special affinity for the peritoneum then we could understand why in the course of bacteremia peritonitis alone might develop and not other metastatic pyemic phenomena, though even such an hypothesis would not explain how the bacteria reach the peritoneum in the absence of an intermediary lesion. The special affinity of bacteria for special tissue is, however, regarded with skepticism by many.

We have collected from the literature one hundred and thirty-six cases that seemed to us more completely studied than usual and that were reported as typical examples of hematogenous peritonitis. In only forty-three of these cases was autopsy performed and none of the postmortem reports mentions a detailed histologic examination of the gastro-intestinal tract. According to our own experience, the source of the peritonitis in this type of case was found only after a careful postmortem examination including a detailed histologic examination of the gastro-intestinal tract. We feel, therefore, that an assumption of a hematogenous origin of peritonitis should never be based on clinical findings, even though the diagnosis is apparently confirmed by an exploratory laparotomy. Clinical reports of cases of peritonitis supposedly hematogenous in origin are, in our opinion, worthless. Similarly, cases reported as hematogenous peritonitis in which autopsy has been performed but in which a complete and careful detailed histologic examination of the entire gastro-intestinal tract and the other peritoneal and retroperitoneal organs has not been made, should not be taken as examples of hematogenous peritonitis.

Some of the cases reported in the literature showed the same type of organisms in the peritoneal exudate and in the circulating blood. This is often considered to be confirmatory evidence of the hematogenous origin of the peritonitis. But here the question arises: propter hoc or post hoc? Steinberg and Goldblatt [13] showed that after the injection of organisms into the peritoneal cavity the same organisms soon appear in the circulating blood. We can, therefore, explain the finding of the same type of organism in the blood and in the peritoneal exudate by the assumption of a secondary invasion of the blood stream from the peritoneal cavity. Experimental evidence would seem to favor this explanation.

To explain the pathogenesis of hematogenous peritonitis, the following assumptions are necessary: First, there must be a primary distant focus of infection, most frequently considered to be the respiratory tract, although any other primary site of inflammation might constitute such a focus. Second, the bacteria from this focus must enter the blood stream primarily or by means of the lymphatics, necessarily producing bacteremia. Third, the bacteria are in some way carried to the peritoneum, there setting up a diffuse inflammation. It is not at all clear how the bacteria enter the peritoneal cavity. Do they leave the smaller vessels or capillaries through the intact endothelial layer, or are they somehow washed out into the peritoneal cavity? We can understand the mechanism that leads to a primary focus of infection and the mechanism of the blood stream involvement. But how the peritoneum becomes infected directly from the circulating blood without an intermediary lesion is difficult for us to grasp. We should have to assume that the bacteria actually lodge in capillaries, forming bacterial emboli and secondary small metastatic abscesses. Or the bacteria might give rise to an infected thrombus with secondary suppuration, and peritonitis, either by direct extension of the infected material into the peritoneal cavity or by an invasion of the peritoneal cavity by bacteria from the infected thrombus through the injured wall of the vessel. But such a peritonitis, even though the causative organisms are traced back to a remote focus and blood stream involvement, in the final analysis, is not the direct result of the blood stream infection. It is caused by the metastatic pyemic abscess in the peritoneal wall or by the infected thrombus that plays the rôle of an abscess and cannot, therefore, be considered an example of so-called hematogenous peritonitis. Peritonitis might occur in this manner, but we must insist on the finding of the intermediary abscess or the infected thrombus. Its occurrence, however, without any evidence of other metastatic pyemic phenomena, is apparently rare.

13. Steinberg, B., and Goldblatt, H.: Studies on Peritonitis, Arch. Int. Med. **39**:446 (March) 1927.

MIGRATORY PERITONITIS

Clinically, the peritonitis in our cases was thought to be hematogenous in origin. At autopsy, however, the peritonitis could be explained by an invasion of the peritoneal cavity by bacteria from an organ either covered by or adjacent to the peritoneum. Cases of peritonitis that occur in this manner are referred to in the German literature as "Durchwanderungs-Peritonitis." The literal translation of the German term Durchwanderungs, "wandering through" being cumbersome, we have adopted the term "migratory," which was suggested by Abt [14] to describe the form of peritonitis caused by the passage of bacteria into the peritoneal cavity from primarily inflamed organs without actual perforation or without direct extension of the inflammatory exudate.

In the cases reported in the literature as migratory peritonitis, the diagnosis seems much less debatable than in those cases in which the peritonitis was considered to be hematogenous in origin. We have collected ninety cases considered to be examples of migratory peritonitis. All of these cases were apparently carefully studied. In sixty-nine of the ninety cases autopsy was performed, as compared with only forty-three autopsies in the one hundred and thirty-six case of peritonitis supposedly hematogenous in origin. Many cases reported as migratory peritonitis showed intestinal lesions without perforation.

Fraenkel,[15] in 1891, showed that bacteria can pass through a nonperforated intestinal wall. He found bacteria in the peritoneal surface of intestinal loops that had been ligated in experimental animals. Flexner,[16] a few years later, found pneumococci in the lumen of the intestines and in the mucosa, submucosa and peritoneum, and called attention to the fact that bacteria may pass through an apparently intact intestinal wall. Hornemann [17] maintained that a migration of bacteria may occur from the intestinal lumen to the peritoneum through the intestinal wall, provided that the wall is diseased. The changes in the intestinal wall, however, may be very slight. Mandl,[18] in 1923, conclusively showed that bacteria can pass through apparently intact intestinal walls.

14. Abt, I.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 3 p. 289; Diagnosis of Peritonitis in Infancy and Childhood, J. Michigan M. Soc. **28**:674, 1929.

15. Fraenkel, A.: Ueber peritoneale Infektion, Wien. klin. Wchnschr. **2**:241, 1891.

16. Flexner, S.: Peritonitis Caused by Invasion of the Micrococcus Lanceolatus from the Intestine, Bull. Johns Hopkins Hosp. **6**:64, 1895; Etiology and Classification of Peritonitis, Philadelphia M. J. **2**:1019, 1898.

17. Hornemann: Beitrag zur Frage ueber die Bakteriendurchlässigkeit der Schleimhaut des Magendarmkanals, Ztschr. f. Hyg. u. Infektionskr. **69**:39, 1911.

18. Mandl, F.: Beitrag zur Frage der kryptogenetischen Peritonitis, Deutsche Ztschr. f. Chir. **182**:289, 1923.

This he demonstrated in patients by placing sterile gauze around loops of intestines that had been sutured to the parietal peritoneum as the first step of a colostomy. Subsequently, and prior to the opening of the intestines, he obtained bacteria of the intestinal flora from this gauze. Jensen,[19] Geinswald [20] and Bail [21] were able to produce peritonitis experimentally by feeding pneumococci and streptococci, respectively.

The concept of migratory peritonitis is based on the presence of a primary inflammation of an organ either within or adjacent to the peritoneal cavity. Most commonly, enteritis is the primary inflammation. This enteritis may be caused by the swallowing of bacteria, especially streptococci, from the throat in cases of an infection of the upper respiratory tract. The low gastric acidity present in acute infectious diseases may be an additional factor in permitting virulent organisms to pass unharmed through the stomach to the intestines (Meyer, Cohen and Carlson [22]). In a large number of our cases the history of an infection of the respiratory tract could be obtained or evidence of such an infection was still present. However, it cannot be denied that this infection might have been merely coincidental and did not play a causative rôle in the production of the enteritis.

The ensuing peritonitis is the result of the invasion of the peritoneal cavity by bacteria from the diseased intestinal mucosa. Gierke [12] maintained that even normal intestines during life may be permeable for bacteria, especially in cases of enteritis. The bacteria may reach the peritoneum by means of the lymphatics, if motile by actual migration through the intestinal wall, or by proliferation with subsequent extension through the intestinal wall. It has also been suggested that bacteria might possibly be carried to the peritoneum by polymorphonuclear leukocytes that migrate through the intestinal wall. It is probable, according to Gierke, that toxins in these cases decrease the resistance of the peritoneum and prepare the way for the bacteria. He, therefore, speaks of a toxic stage of this type of peritonitis. According to Abt,[14] the permeability of the intestinal wall is markedly increased during nutritional disturbances, and micro-organisms may wander through it. He further stated that Tobler and Bessau considered it improbable that the pathologic permeability of the gastro-

19. Jensen, J.: Ueber Pneumokokken Peritonitis, Arch. f. klin. Chir. **70**:91, 1903.

20. Geinswald, quoted by Mandl (footnote 18).

21. Bail, M.: Die Schleimhaut des Magendarmtractes als Eingangsporte pyogener Infektionen, Arch. f. klin. Chir. **62**:369, 1900.

22. Meyer, J.; Cohen, S. J., and Carlson, A. J.: Contribution to the Physiology of the Stomach, Arch. Int. Med. **21**:354 (March) 1918.

intestinal mucosa is a result of bacterial poisons of the intestinal content but were more inclined to believe that the volatile fatty acids cause an increased permeability.

In only a relatively small number of cases of enteritis, however, does migratory peritonitis develop, because the peritoneum, under normal conditions, is so resistant that, even though it is invaded by bacteria, peritonitis does not develop. In their experiments, Steinberg and Goldblatt [17] were unable to produce peritonitis in dogs by the injection of bacteria alone into the peritoneal cavity.

If, however, in cases of enteritis, peritonitis does develop, such an occurrence may be explained in several ways. It may depend on the presence of a specially virulent strain of bacteria whether or not peritonitis results. In eight of our cases of enteritis, streptococci were obtained from cultures and in one case they were found in smears of the peritoneal exudate. In one case pneumococci were found in cultures, and in another case in smears from the peritoneal exudate and the intestinal lumen. Most of the case reports mention the finding of either streptococci or pneumococci. It seems conceivable that the peritonitis in our cases and in similar cases, because of the normal resistance of the peritoneum, is not the result of a single or occasional invasion of the peritoneal cavity by bacteria. Repeated invasions, however, may lower the resistance of the peritoneum to such an extent that it finally reacts with an inflammation. Furthermore, the coincidental occurrence of a disturbance in feeding, of an acute illness such as an infection of the upper respiratory tract or of a chronic debilitating disease may lower the resistance of the patient to such a degree that bacteria that have passed from the diseased intestinal mucosa into the peritoneal cavity may produce peritonitis. It is also possible that insignificant traumas of the abdomen in young children lower the resistance of the peritoneum and make it susceptible to the action of invading organisms. These traumas may be so mild as to escape notice. Such an explanation seems plausible because of the fact that nonperforating traumas of the abdominal wall have been known to produce a migratory peritonitis in apparently healthy persons who revealed no evidence of enteritis (Kaufmann,[10] Hertzler [23]).

Flexner [16] stated that the existence of chronic inflammatory changes such as thickenings of the peritoneal coat and adhesions between neighboring viscera is certainly not inconsistent with the assumption of an abnormal or lessened vital resistance in these parts. He further stated that it would seem as if two conditions, namely, the opportunity for the escape from the interior of the intestines of soluble chemical sub-

23. Hertzler, A. E.: The Peritoneum, St. Louis, C. V. Mosby Company, 1921.

stances (products of the growth of bacteria) into the abdominal cavity and the preexistence of chronic inflammatory changes, might become important factors in the development of the peritonitis, the presence of the infecting micro-organisms being assumed.

In this connection, it is of interest to mention that Erdheim [24] recently expressed the belief that a diagnosis of hematogenous peritonitis made at the autopsy table is a confession of the pathologist that he did not find the cause of the peritonitis.

We shall say just a few words as to the so-called pneumococci peritonitis. This type of peritonitis, if it occurs in females, might be explained in some instances by a direct extension of pneumococci from the vagina, uterus and tubes into the peritoneal cavity (McCartney and Fraser,[8] and McCartney [25]). In other instances this peritonitis may be a migratory peritonitis with primary lesions in the intestinal tract or pulmonary pleura. The presence of pneumococci in the intestinal lumen or in the feces has been demonstrated by Jensen,[19] Flexner [16] and others. In one of our cases, we were able to obtain pneumococci from the intestinal lumen and peritoneal exudate. The pneumococcic peritonitis in cases of lipoid nephrosis may also be explained as a migratory peritonitis. The chronic ascites in such cases might lower the resistance of the peritoneum and render it susceptible to subsequent invasion by bacteria.

CONCLUSIONS

1. Twenty-four cases of peritonitis, twenty-one of which were diagnosed clinically as hematogenous peritonitis, proved at autopsy to be the result of an invasion of the peritoneal cavity by bacteria from primarily diseased intraperitoneal organs or structures close to the peritoneum, without perforation or without direct extension of the inflammatory process to the peritoneum. Sixteen of the twenty-four cases showed enteritis.

2. The term "migratory peritonitis" seems appropriate for this type of case, because it corresponds with the German term "Durchwanderungs-Peritonitis" and signifies the pathogenesis of this form of peritonitis.

3. Clinical reports of cases of hematogenous peritonitis without autopsies, or with autopsies but without complete histologic examination of the gastro-intestinal tract, such as comprise the bulk of the literature of so-called hematogenous peritonitis, should be discarded.

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24. Erdheim, J.: Personal communication to Dr. Saphir.

25. McCartney, J. E.: The Pathogenesis of Primary Pneumococcal Peritonitis, J. Path. & Bact. **26**:507, 1923.

4. Many of the cases in which the condition was reported as hematogenous peritonitis are examples of migratory peritonitis.

5. The evidence supporting the occurrence of peritonitis directly following a blood stream infection without an intermediary lesion within or adjacent to the peritoneal cavity is inadequate.

6. From our observations, it is apparent that so-called hematogenous peritonitis may occur as part of a generalized metastatic pyemic process that results in abscess formation or infected thrombi within or adjacent to the peritoneal cavity. The ensuing peritonitis is the direct result of the abscess or thrombus. It is unlikely, however, that this form of peritonitis does occur in the absence of other metastatic pyemic phenomena.

PYURIA AND PYELITIS

THE INFLUENCE OF EXSICCOSIS ON THEIR EXPERIMENTAL PRODUCTION *

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In spite of intensive clinical and experimental study, much uncertainty still surrounds the related subjects of pyuria and pyelitis, particularly as they occur in childhood. The greatest disagreement concerns the route by which infection reaches the renal pelvis. It was formerly considered practically impossible to establish infection of the kidney by introducing organisms into the bladder of a normal animal. However, Helmholz and Beeler [1] were able to produce pyelitis in a large proportion of rabbits, both by intracystic and by intravenous injection of colon bacilli that had developed to a striking degree the property of selective localization. These experiments establish the possibility of two routes of infection, but leave open the questions of how organisms reach the bladder and what route they follow from there to the kidney.

Further investigation is necessary. The observations of Helmholz and Beeler are valuable, but their method has the disadvantage, for continued research, that such nephrotropic organisms as they saw are rarely encountered, and gradually lose their special affinity for the kidney. Helmholz [2] found only three such strains in ten years. A dependable technic for producing experimental pyelitis would seem to be a prerequisite for any intensive study of this subject.

Abnormal urine has resulted from several indirect experimental methods, which can be utilized for further studies. Sweet and Stewart [3] consistently found ascending infection in dogs after anastomosing the ureter with the bowel. Bradford [4] has studied by cultural methods the

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1. Helmholz, H. F., and Beeler, Carol: Experimental Pyelitis in the Rabbit, J. A. M. A. **69**:898 (Sept. 15) 1917; Experimental Pyelitis in the Rabbit, J. Urol. **2**:395 (Oct.) 1918.

2. Helmholz, H. F.: The Production of Local Renal Lesions in Rabbits by Intravenous Injections of Certain Strains of B. Coli, J. Infect. Dis. **41**:448 (Dec.) 1927.

3. Sweet, J. E., and Stewart, L. F.: The Ascending Infection of the Kidneys, Surg., Gynec. & Obst. **18**:460 (April) 1914.

4. Bradford, W. L.: Mucosus Organism from Suppurative Lesions of Rat on Diet Deficient in Vitamin A, J. Infect. Dis. **43**:407 (Nov.) 1928.

urinary infection that frequently develops in rats receiving a diet deficient in vitamin A. Pyuria secondary to loss of water has been described by Schiff and his co-workers [5] and investigated further by Kramár.[6] Helmholz has recently discovered a fourth method, which I shall report in detail, together with some experiments in which this technic was used.

In the course of a study of the diuretic effect on rabbits of infusions of 20 per cent solution of sucrose, Helmholz noticed that the urine of the animals sometimes contained large numbers of leukocytes. In view of the work of Schiff and Bayer, Kramár [7] and others, it was thought that this was probably the result of loss of water. The powerful diuretic effect of infusions of sucrose furnished a reasonable basis for this hypothesis, which has not, however, been supported by subsequent observations.

An idea of the diuretic possibilities of such infusions can be given by figures for the rates of injection and secretion in a few of the animals. Regardless of the actual duration of the experiment, these figures express amounts of the solution injected and of the urine excreted in cubic centimeters for each hour for each kilogram of the rabbit's weight. Thus in one rabbit, infusion occurred at the rate of 93 cc. an hour, and excretion at the rate of 116 cc. an hour, for each kilogram of body weight; on another occasion, the intake was 88 cc. and the output 102 cc. It was not always possible to inject the sucrose so fast. For instance, the rates per hour in two experiments on rabbit 39 were 40 cc. and 30 cc. for infusion and 16 cc. and 18 cc. for excretion. In another animal the average rate per hour of eight injections was 38 cc.; the average rate of excretion, 34 cc.

Since the experiments were not planned to show the degree of diuresis, different rates of infusion were used. However, a constant rate of infusion was usually maintained for a single experiment by the use of a Woodyatt pump. The duration of the injections also varied, for while most of them were continued for one hour, and later two hours, they sometimes had to be discontinued before the time was

5. Schiff, E.: Bemerkungen zu der Arbeit M. Franks: Die Pathogenese der Säuglingspyurie, Arch. f. Kinderh. **79**:105, 1926. Schiff, E., and Bayer, W.: Zur Pathogenese der Ernährungsstörungen beim Säugling: Das Nierensyndrom; Dehydrationspyurie, -zylindrurie, und -albuminurie, Jahrb. f. Kinderh. **108**:157, 1925. Schiff, E.; Bayer, W., and Choremis, K.: Zur Pathogenese der Ernährungsstörungen beim Säugling: Experimentelle Exsikkose und Leberglykogen, ibid. **109**:287, 1925.

6. Kramár, Eugen: Untersuchungen über die Pathologie der Säuglingsintoxikation: Die experimentelle Intoxikation, Jahrb. f. Kinderh. **114**:356, 1926; Untersuchungen über die Pathologie der Säuglingsintoxikation: Die Rolle des Eiweisses, ibid. **115**:289, 1927.

7. Kramár (footnote 6, first reference).

up. At the beginning and end of the experiment, the animals were catheterized, so the exact amount of urine excreted during the experimental period was known. The subsequent output was not measured, but it was observed that diuresis continued for some time. The effect of this was more noticeable because, following injection, the animals temporarily refused food and water. Additional injections were given, usually at intervals of from three to five days, as long as the rabbits lived.

A bacteriologic study of the urine was not part of the original plan, and only after the work had been in progress for some time were cultures taken. In most of the cases of pyuria, the urine was

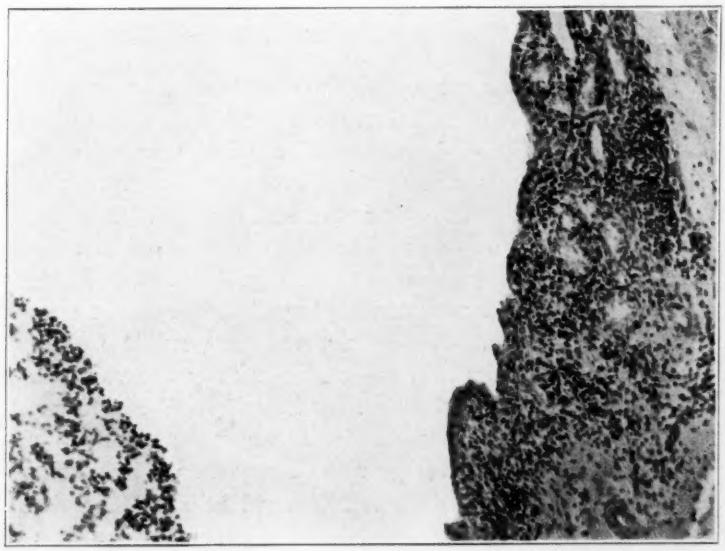

Fig. 1 (rabbit 8).—Pus in the renal pelvis and massive infiltration of its wall; × 100.

then found to contain gram-negative rods which had the cultural properties of colon bacilli. In most instances, large numbers of colonies grew on litmus-lactose-agar plates from 0.5 cc. of urine. After this observation, the animals were studied more from the point of view of infection of the urinary tract, and cultures were taken as a routine.

At necropsy, the kidneys were removed intact, and fixed in a diluted solution of formaldehyde, U. S. P. (1:10): Sections were cut transversely through the entire organ, including the pelvis. This technic makes it possible to see at once the relations of lesions to the cortex, medulla, papilla, both walls of the pelvis and the peripelvic fat.[8]

8. Helmholz, H. F.: The Pathologic Changes in Experimental, Ascending and Hematogenous Pyelitis, J. Urol. **8**:301 (Oct.) 1922.

Leukocytic infiltration of the lining of the pelvis was seen in fourteen cases; it was usually limited to the parietal pelvic wall. In one section, a small, localized inflammatory area was seen in the epithelium at the tip of the papilla; however, this condition was not found again. The greatest infiltration was in the part of the lining membrane that folds over a finger-like process of peripelvic connective tissue projecting into the lateral parts of the pelvic cavity. Regions of infiltration in the peripelvic fat were seen in half of the cases of pyelitis, corresponding roughly in amount with the degree to which the pelvic wall was affected (figs. 1, 2 and 3).

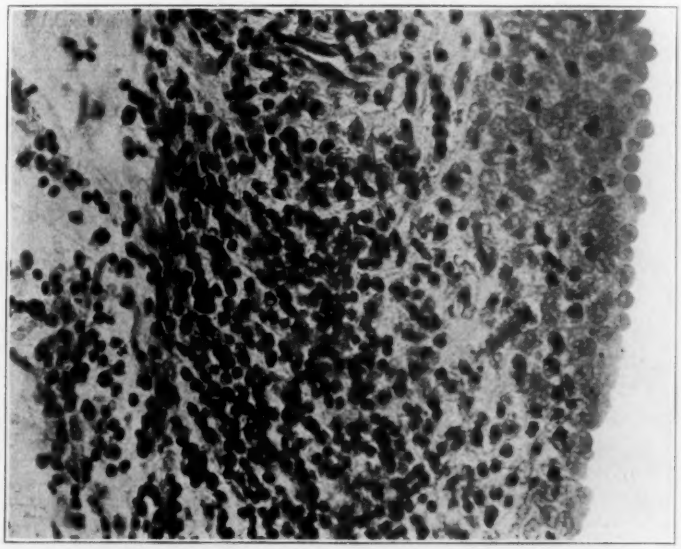

Fig. 2 (rabbit 8).—Polymorphonuclear and lymphocytic infiltration; × 325.

The situation of the inflammatory reaction agrees with that seen by Helmholz [8] in experimental ascending pyelitis, and is in sharp contrast to his observations in hematogenous infections. In all but two of twenty rabbits in which pyelitis developed from intravenous injections of colon bacilli, he found the renal substance involved in the disease process.

Table 1 summarizes the observations in group 1, consisting of the rabbits that had pyelitis. Examination of the urine had not been begun at the time of the first five experiments. Tests of renal function with phenolsulphonphthalein were made over a period of four hours in most instances, and they gave evidence of reduced function only late in the disease. This is related to the parenchymatous changes, however, which will be reported separately. In some animals the left kidney

was removed for comparison later with the remaining experimentally injured kidney. This may have influenced the development of pyelitis by increasing the work of the remaining organ.

Table 2 summarizes data on group 2, consisting of thirty-one rabbits in which acute pyelitis was not demonstrated histologically. Histologic study of the four animals that had both pyuria and bacilluria revealed cystitis in one and chronic infection of the renal pelvis in another. A third had leukocytic infiltration of the peripelvic tissues, which was also observed in one of the first animals of the series, of which the urine was never analyzed. The occurrence of this inflammatory reaction, like that seen in half the rabbits in group 1, suggests that these two animals may have had slight changes of the pelvic lining which did

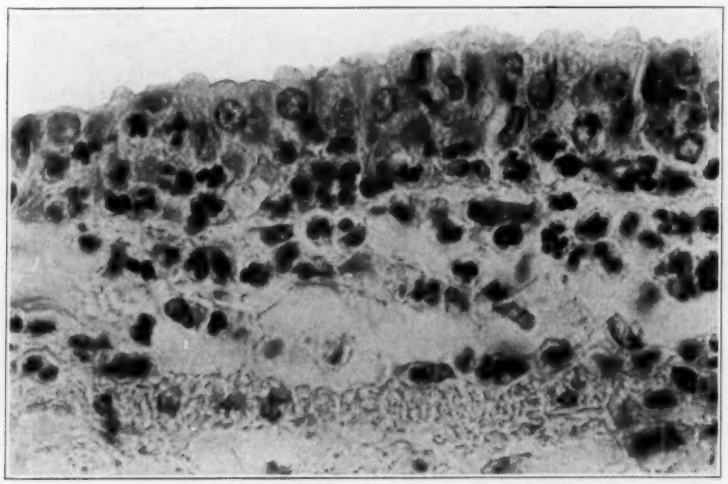

Fig. 3 (rabbit 12).—Polymorphonuclear leukocytes in the lining membrane of the renal pelvis and extending out into the peripelvic tissue; × 700.

not appear at the level of the sections. A comparison of the two groups shows that the likelihood of renal lesions developing was increased by the continued survival of the animal as well as by further injections.

I am unable to explain the occurrence of pyelitis following injections of sucrose. Repeated catheterization does not infect the urinary tract of a rabbit. Even by the injection of colon bacilli into the uninjured bladder it is almost impossible to produce pyelitis, unless the organisms have developed special affinity for the urinary tract.[9] Infection by intracystic inoculation can be produced with the aid of some accessory factor that lowers local or general resistance, such as a previous injection of turpentine.[10] However, my animals were carefully

9. Helmholz and Beeler (footnote 1, second reference).
10. Hess, quoted by Helmholz and Beeler (footnote 1, second reference).

catheterized, and there was never any gross hematuria or other indication of injury. The solutions of sucrose used were sterile, prepared in the same laboratory as all the solutions used for intravenous injections that are supplied to a large hospital. One possible factor, that of exsiccosis, was difficult to evaluate. To gain more information on this point, I carried out a series of experiments on animals.

Schiff and his associates,[11] Frank,[12] and Kramár and his associates [13] have contributed to the subject. It has been generally assumed that

TABLE 1.—*Injections of Sucrose Into Rabbits in Which Pyelitis Developed*

									Histologic Examination			
Rabbit	Sex	Injections	Days to Necropsy	Days to First Positive Culture	Degree of Infection*	Days to Onset of Pyuria	Amount of Pus in Catheterized Urine*	Phenolsulphonphthalein Test, per Cent	Pus in Pelvis	Infiltration of Pelvic Wall	Peripelvic Infiltration	Comment
1	M	5	69	66	1	66	4	...	0	1	0	
2	?	6	18	..	..	..	..	...	0	1	1	Left kidney removed before injection
3	M	3	10	..	..	..	..	...	3	3	2	Both kidneys affected
4	M	8	19	..	..	10	4	3	4	4	3	
5	?	4	9	..	..	..	..	64 48	2	2	2	
6	F	5	19	..	..	..	..	100	2	3	0	Left kidney removed before injection
7	?	6	42	40	1	40	4	100 75 5	1	1	0	Left kidney removed before injection
8	F	7	80	48	1	48	4	50	4	4	3	Left kidney removed before injection
9	F	5	22	..	0	..	0	...	1	1	0	Postmortem changes obscured results
10	F	6	33	27	1	27	4	...	4	4	2	
11	M	4	16	10	1	10	4	5	3	2	0	Definite cystitis present
12	F	4	18	18	1	18	4	5 15	4	4	0	Left kidney removed before injection
13	M	15	97	16	4	16	4	...	0	2	1	
14	M	13	106	3	4	14	3	75 90 92 74	0	2	2	Left kidney removed before injection

* Graded on a basis of 0 to 4 in all tables.

11. Schiff et al. (footnote 5); Das Exsiccoseproblem, Ergebn. d. inn. Med. u. Kinderh. **35**:519, 1929; Zur Pathogenese der Ernährungsstörung beim Säugling: Experimentelle Exsikkose und ihre Beziehung zum Toxikose-Problem, Jahrb. f. Kinderh. **106**:263, 1924.

12. Frank, Max: Die Pathogenese der Säuglingspyurie: Klinische, bacteriologische, anatomische und tierexperimentelle Studien, Arch. f. Kinderh. **77**:264 (March) 1926.

13. Kramár (footnote 6). Kramár, Eugen; and Kovács, Andreas: Untersuchungen über die Pathologie der Säuglingsintoxikation: Pathologisch-anatomische Beobachtungen bei der experimentellen Intoxikation und Exsikkose, Jahrb. f. Kinderh. **118**:94, 1927.

pyuria associated with loss of water is not the result of an infectious process. Little direct evidence has been presented to prove this point. Beeler and Helmholz [14] reported two cases in which infants had highly concentrated urine, containing many leukocytes and moderate numbers of erythrocytes and casts. On culture, too few organisms were found for a diagnosis of bacilluria. Schwartz [15] observed similar signs in children with extra-urinary infections, and warned that this does not neces-

TABLE 2.—*Injections of Sucrose Into Rabbits in Which Pyelitis Did Not Develop*

Rabbit	Sex	Injections	Days to Necropsy	Days to First Positive Culture	Degree of Infection	Days to Onset of Pyuria	Amount of Pus in Catheterized Urine	Comment
15	M	6	20	..	*	..	†	Left kidney removed before injection
16	F	4	6	..	*	..	†	Chronic infiltration of pelvic wall and peripelvic tissues
17	M	2	4	..	*	..	†	Peripelvic infiltration, graded 3
18	F	4	13	..	*	..	†	
19	M	3	7	..	*	..	†	
20	F	6	16	..	*	10	4	Left kidney removed before injection
21	M	7	34	..	0	..	0	Postmortem changes obscured result
22	M	5	26	..	*	19	2	
23	M	2	7	..	0	..	0	
24	M	4	20	..	0	5	1	
25	F	6	29	..	0	..	0	
26	F	2	7	..	*	..	†	
27	F	2	5	5	1	..	†	Postmortem changes obscured result
28	M	8	40	40	4	..	0	
29	F	4	15	14	1	..	†	
30	M	2	5	5	1	..	†	
31	F	3	7	..	0	..	0	
32	F	12	62	..	0	..	0	Renal function, 75 per cent in four hours
33	F	10	62	..	0	..	0	Renal function, 75 per cent in four hours
34	F	3	12	..	0	..	0	
35	M	2	6	..	*	..	†	
36	M	10	47	47	4	..	0	
37	M	2	5	5	4	5	4	Postmortem changes obscured result
38	F	3	17	17	4	17	4	
39	F	3	34	..	0	26	2	Renal function, 75 per cent in four hours
40	F	3	27	..	0	..	†	
41	F	4	9	..	0	..	0	Left kidney removed before injection
42	M	4	14	14	4	14	4	Cystitis; renal function, 75 per cent in four hours
43	M	2	6	..	0	..	0	
44	F	2	3	3	1	3	2	Renal function, 75 and 100 per cent in four hours on different days; peripelvic infiltration, graded 3
45	F	3	13	..	0	..	0	Renal function 80 and 90 per cent in four hours on different days

* Cultures not made.
† Not examined.

sarily imply pyelocystitis, for the urine may be sterile. Indeed, without catheterization, it is not always possible to be certain that the cells found in the urine come from the bladder. Schiff [16] denied that sterile pyuria

14. Beeler, Carol, and Helmholz, H. F.: The Bacteriology of the Urine in Healthy Children and Those Suffering from Extra-Urinary Infections, Am. J. Dis. Child. **12**:345 (Oct.) 1916.

15. Schwartz, A. B.: The Bacteriology of the Urine in Children with Gastro-Intestinal Diseases, Arch. Pediat. **35**:1 (Jan.) 1918.

16. Schiff (footnote 5, first reference).

must be the result of aseptic inflammation. He felt that there is not necessarily an anatomic change, but he did not explain how or where the cells gain access to the urine. Faerber [17] even suggested that these cells are not leukocytes at all, but wandering cells from the tissues. This view has not met with general acceptance.

By observations on animals with restricted intake of water, I hoped to determine whether pyuria occurring in exsiccosis was the result of infection, and to discover, if possible, the source of the leukocytes in the urine. It was proposed to do this by separate microscopic and cultural examinations of urine from the bladder and from each renal pelvis, followed by histologic study of the urinary organs. Aseptic catheterization is technically difficult in the smaller laboratory animals, and would invite the criticism that any organisms found had been carried in by the catheter. It was therefore decided to dispatch the animals when exsiccosis was well established, and to take the cultures at necropsy by introducing sterile pipets into the bladder and renal pelvis through seared surfaces.

Intoxication (Finkelstein [18]) is a disease of infancy; therefore, young animals should be selected for its experimental production. Because rabbits of the proper age are extremely delicate, my first experiments were performed on white rats. Their weight ranged from 12 to 37 Gm., with a mean of 26.4 Gm. Lowrey [19] gave the average weight of the albino rat at 20 days as 24.5 Gm., and Donaldson [20] stated that the young can be weaned at 21 or 22 days, but usually suckle a few days longer if they are left with the mother. The size of the rats varies with the stock and the conditions under which they are raised, but the foregoing figures are sufficient to show that our average animal was about at the weaning period.

Young rats of both sexes were fed a stock diet that contained, in round numbers: cornmeal, 55 per cent; linseed meal, 12 per cent; crude casein, 4 per cent; alfalfa, 14 per cent; salt, 4 per cent; calcium carbonate, 4 per cent, and powdered skim milk, 7 per cent. On this food the animals rapidly lost weight and strength and seldom survived the fifth day. They failed to show the signs of intoxication as described by Kramár [7] in the dog, but presented much the same picture as the puppies in which exsiccosis developed when they were given a diet free from protein. I was anxious to allow as much time as possible for the development of pyuria. Therefore, the rats were dispatched

17. Faerber, Ernst: Neuer Anschauungen über die Albuminurie und Pyurie im Kindesalter, Ztschr. f. Urol. **21**:7, 1927.

18. Finkelstein, quoted by Schiff and Bayer (footnote 5, second reference).

19. Lowrey, quoted by Donaldson (footnote 20).

20. Donaldson, H. H.: The Rat: Data and Reference Tables, Memoirs Wistar Institute of Anatomy and Biology, ed. 2, Philadelphia, 1924, no. 6.

only when they appeared unable to survive the night. As a result, some of them were found dead in the cage in the morning, and the organisms recovered from the urine were probably postmortem invaders. However, this fact is of little consequence, since pyuria failed to develop, and since the cultures were intended primarily to indicate whether infection was responsible for the pyuria which has been described in exsiccosis.

Eight of the rats were given daily a few drops of castor oil, which produced moderate diarrhea in some animals, but which did not appear appreciably to increase the rate of loss of water. Another reason for giving the oil was that diarrhea should increase the possibility of colon bacilli reaching and ascending the urethra. Also, Smith [21] has stated, without any convincing proof, that many cases of pyelitis in the female are due to bacteria entering the lymphatics from the urethra, vulva and vagina.

Table 3 summarizes the experimental results obtained in twenty-three rats. Cultures of the blood and of urine from the bladder were taken in dextrose-brain broth. Escherichia coli or a coccus grew so regularly in the cultures from animals that were found dead that finally bacteriologic examination was undertaken only when it was possible immediately after death.

When it became apparent that pyuria did not develop in young rats as a result of decreased ingestion of water, even with a normal intake of protein, I started similar experiments with guinea-pigs. The series consisted of twelve animals of both sexes, approximately from 2 to 3 weeks old, and weighing between 118 and 232 Gm. They were given a diet of grain, supplemented in three instances with a little alfalfa. On this ration, which contained adequate protein, the guinea-pigs survived for from five to nine days without any signs of intoxication. Five were found dead, and the others were chloroformed when death appeared imminent. The length of survival was greater in the larger guinea-pigs. Loss of weight of five animals was recorded to the time of necropsy, and averaged 36.1 per cent.

In table 4 are summarized the results of experiments on guinea-pigs. The cultures of the urine from the bladder were taken in dextrose-brain broth, and also, for the first eight animals, in litmus-lactose agar, which was then poured into plates. It was possible to culture urine from the renal pelvis of eight animals. A colon bacillus was isolated from the urine of the bladder twice, but only two and three colonies grew on the agar plates, which is insufficient to warrant the belief that bacilluria existed. A streptococcus was found in the urine

21. Smith, R. M.: Pyelitis of Infancy: I. Mode of Infection, Am. J. Dis. Child. **12**:235 (Sept.) 1916.

of the bladder of one animal, but plates had not been inoculated; therefore, the degree of infection was not known. A streptococcus grew from urine of the left renal pelvis, but not from that of the right. In this animal, as in three others, the ureters had been tied under ether anesthesia, one to two hours before death. The renal pelvis did not fill enough in this time appreciably to facilitate the taking of cultures,

TABLE 3.—*Data on Experiments in Restriction of Water Applied to the Rat*

Rat	Weight, Gm.	Loss of Weight, per Cent	Days to Necropsy	Microscopic Examination of Urine	Cultures‡		Comment‖
					Urine from Bladder	Blood	
1	24.0	33	3 chloroformed	Occasional leukocyte	Hay bacillus	Hay bacillus	
2	23.0	22	5	No abnormality	Streptococcus; Escherichia coli	No growth	
3	16.0	..	3	No abnormality	Staphylococcus	No growth	
4	17.5*	..	3	Occasional leukocyte	Staphylococcus	Streptococcus	
5	33.0	26	10 chloroformed*	No abnormality	No growth	No growth	Castor oil administered
6	28.1	34	4 chloroformed	No abnormality	No growth	No growth	Castor oil administered
7	29.9	41	6 chloroformed*	Not made	No growth	No growth	Castor oil administered
8	27.6	41	6†	Not made	Escherichia coli; large gram-positive rods	Escherichia coli; large gram-positive rods	Castor oil administered
9	26.9	39	6†	Not made	Few Escherichia coli; streptococcus	Few Escherichia coli; streptococci	Castor oil administered
10	28.7	..	3	Not made	No growth	Not made	Castor oil administered
11	10.5	8	3	No abnormality	Escherichia coli	Escherichia coli	Castor oil administered
12	12.0*	17	4	Not made	Escherichia coli; streptococci; gram-positive rods	Escherichia coli; streptococci	Castor oil administered
13	19.9	25	4 chloroformed	Not made	No growth	Not made	
14	30.6	28	4	No abnormality	No growth	No growth	
15	32.6	29	4	Not made	Escherichia coli; streptococci	Escherichia coli; few diplococci	
16	26.0	..	4	Not made	Not made	Not made	
17	31.5	..	5	Not made	Not made	Not made	
18	27.0	..	4	Not made	Not made	Not made	
19	26.5	..	4	Not made	Not made	Not made	
20	34.5	41	5	Occasional leukocyte	Not made	Not made	
21	32.5	..	4	Not made	No growth	No growth	
22	37.0	35	5 chloroformed	Not made	No growth	No growth	
23	31.0	..	4 chloroformed	Not made	No growth	No growth	

* Weighed on second day.
† Accidentally received extra fluid.
‡ Urine was obtained from the renal pelvis of rats 14, 15 and 23 only; of these specimens of urine only that from the left renal pelvis of rat 15 contained organisms, streptococci.
‖ Histologic changes in the kidney or bladder were not found. Sections from the bladders of rats 2, 3 and 4 were not obtained.

but the ureters were a little distended. Urine was obtained from the left ureter for a culture which was negative, so the streptococcus was probably a contaminant. It is of interest that there was no growth in cultures from guinea-pig 8, the one animal that had pyuria, or from guinea-pig 12, in the urine of which bacteria were visible.

Sections of the entire kidney and of the bladder were examined and were entirely normal, as in the rats.

Similar experiments were carried out on two male dogs, aged about 10 to 14 days. One weighed 680 Gm.; the other, 876 Gm. Beginning February 13, they were given a diet similar to that used by Kramár.[7] It seemed simpler to make an equivalent mixture with dried milk powder than to evaporate whole milk to one-fourth its volume. Twenty per

TABLE 4.—*Data on Experiments in Restriction of Water Applied to the Guinea-Pig* *

Guinea-Pig	Weight, Gm.	Loss of Weight, per Cent	Days to Necropsy	Microscopic Examination of Urine	Cultures			
					Urine from the Bladder	Urine from Pelves		Blood
						Right	Left	
1	161	32	8 chloroformed	No abnormality	No growth	Not made	Not made	No growth
2	163	29	8 chloroformed	Occasional leukocyte	No growth	Not made	Not made	No growth
3	134	..	6	No abnormality	Escherichia coli, 2 colonies	No growth	No growth	Escherichia coli, streptococci; gram-positive rods
4	133	..	7	No abnormality	No growth	No growth	No growth	No growth
5	175	..	6	Three leukocytes, many casts, 3 erythrocytes in a high dry field	No growth	No growth	No growth	No growth
6	169	..	7	No abnormality	Escherichia coli; 3 colonies	Escherichia coli	No growth	No growth
7	230	..	7 chloroformed	No abnormality	No growth	No growth	Gram-negative rods end to end	Gram-negative rods end to end
8	220	..	7 chloroformed	Pus graded 4	No growth	No growth	No growth	Escherichia coli
9	232	43	9 chloroformed	Not made	No growth	Not made	No growth	No growth
10	134	..	6 chloroformed	Not made	Streptococci	No growth	Streptococci†	Gram-negative diphtheroids
11	118	31	5	No abnormality	No growth	Not made	Not made	No growth
12	134	31	7 chloroformed	Occasional leukocyte; bacteria, yeast (?)	No growth	Not made	Not made	No growth

* All sections of the kidney and bladder were normal histologically.
† Cultures of urine from the left ureter gave negative results.

cent sucrose was added, which was half the amount used by Kramár in his first experiments, but double the content of the standard diet described in his second article.[22] This food was given ad libitum and was well taken.

On February 16, the smaller animal did not eat well, and the next morning both dogs exhibited the signs of intoxication described by Kramár.[7] They had no fever, but they appeared exhausted and were unwilling to eat. Vomiting and slight diarrhea were noted later. On

22. Kramár (footnote 6, second reference).

February 20, the smaller animal weighed 484 Gm., and was chloroformed. The other dog died in the night. Neither leukocytes nor casts were found in the urine from the bladder of either animal. Cultures of urine from the bladder and from the pelvis of all of the kidneys and cultures of the blood were negative. Sections of the bladder, ureter and both kidneys were examined; all signs of inflammation were lacking.

Sections of liver and kidney were stained for fat. Scarlet red stain revealed considerable fatty infiltration of the liver and fine droplets in the tubular epithelium of the kidney. This was more conspicuous in the convoluted tubules, in which Kramár and Kovács [23] found fat, but the condition was seen also in the straight tubules.

COMMENT

In spite of advanced exsiccosis, only one instance of pyuria was found among the eleven rats, ten guinea-pigs and two dogs from which sufficient urine was obtained for microscopic examination. Schiff and Bayer have observed a "kidney syndrome" usually occurring in infants whose intake of fluid was limited, and Kramár [7] made the same observation on dogs. The failure of these authors to obtain by catheterization the specimens of urine that they examined makes their results less valuable. However, similar observations have been made in the presence of loss of water in acute infections by Beeler and Helmholz and by Schwartz, who examined catheterized specimens. It is not possible to draw conclusions too freely about one species from experiments made on others, but these observations indicate the need for caution in accepting Schiff's belief that purely functional changes will cause true pyuria.

In view of the statement of Kramár and Kovács that fatty infiltration of the liver and the kidneys is sometimes found in normal dogs, significance cannot be attached to its occurrence in my experimental animals. The failure to find any microscopic evidence of pyelitis in thirty-five animals that were in a state of exsiccosis makes it seem improbable that loss of water alone could have been responsible for the urinary infections induced by injections of sucrose.

The positive cultures of urine and blood taken from the animals found dead must be considered due to postmortem contamination.

SUMMARY AND CONCLUSIONS

Pyelitis was produced in fourteen of forty-five rabbits by infusions of 20 per cent solution of sucrose. In thirteen of twenty-eight animals

23. Kramár and Kovács (footnote 13, second reference).

that had received four or more injections, pyelitis developed. Repeated injections and longer survival of the animals increased the incidence of urinary infections.

The situation of the inflammation in the lining of the pelvis and the absence of cortical abscesses are strong evidence that the lesions were due to ascending infection. There is no evidence to show whether this occurred by way of the lumen of the ureter or the accompanying lymphatic channels.

Some possible explanations of these observations are considered. A logical conclusion is that the injection of sucrose has lowered the resistance of the kidneys to infection. That this can result from a decreased water content of the body was shown in mice by Schiff. The mechanism by which this lowered resistance is brought about is not known.

The effect of decreased intake of water was studied in rats, guinea-pigs and dogs. In spite of rigorous restriction of fluids, pyuria was observed only once, in a guinea-pig without bacilluria. There was no histologic evidence of inflammation of the urinary tract in any of the animals. From these observations, it seems improbable that withdrawal of water from the tissues alone was responsible for the pyelitis produced in rabbits. The symptoms of toxicosis as described by Kramár appeared only in the two dogs, but in these animals pyuria did not develop. Definite conclusions cannot be drawn from so few experiments. It has been established, however, that a similar picture does not result in rats or guinea-pigs. Pyuria occurred only once in these animals, and thus it seems improbable that it was related to the exsiccosis.

Case Reports

HEMOLYTIC JAUNDICE NOT INFLUENCED BY SPLENECTOMY *

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Micheli,[1] in 1911, was the first to report a case of acquired hemolytic icterus in which splenectomy was performed, with the result that the jaundice and anemia disappeared completely. In 1913, Kahn,[2] Wynther [3] and Thursfield [4] recorded similar success in cases of congenital hemolytic jaundice. Since then, more favorable reports have been published in a large series of cases, and today removal of the spleen is recognized as the accepted therapeutic procedure for patients with hemolytic jaundice. Giffin,[5] reporting on eighty-one cases in which splenectomy was performed at the Mayo Clinic, emphasized the value of the operation and concluded that "in two diseases, hemolytic jaundice and hemorrhagic purpura, the indication for splenectomy depends almost entirely on a satisfactory diagnosis." The number of unfavorable results of the operation is not high. The mortality in Giffin's series was 4.93 per cent.

In a consideration of the unfavorable results of splenectomy, one must separate the cases in which death was due to operative shock or a subsequent, intercurrent disease and those in which the hemolytic process was not arrested by the splenectomy. It is known that the increased fragility of the erythrocytes and the microcytosis occasionally continue after the operation, but such observations receive only theoretical attention and are not considered of great practical importance because the improvement of the clinical symptoms of jaundice and anemia is so striking. There are cases on record in which the symptoms recurred

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* From the Pediatric Service and the Division of Laboratories of Mount Sinai Hospital.

1. Micheli, F.: Unmittelbare Effecte der Splenectomie bei einem Fall von erworbenem hämolytischen splenomegalischen Ikterus Typus Hayem Widal (Spleno-Hemolytischer Ikterus), Wien. klin. Wchnschr. **24**:1269 (Sept. 7) 1911.

2. Kahn, F.: Ueber hämolytischen Ikterus und seine Beeinflussung durch Splenectomie, Verhandl. d. deutsch. Kong. f. inn. Med. **30**:327, 1913.

3. Wynther, W. Essex: Case of Acholuric Jaundice After Splenectomy, Proc. Roy. Soc. Med. (Clin. Sect.) **6**:80, 1913.

4. Thursfield, in discussion on Wynther (footnote 3, p. 81).

5. Giffin, Herbert: Splenectomy, Surg., Gynec. & Obst. **45**:577 (Nov.) 1927.

following operation, or in which the hemolytic process was not only not arrested by the removal of the spleen, but grew progressively worse.

Occasional attacks of jaundice after splenectomy have been reported.

REPORT OF CASES FROM THE LITERATURE

CASE 1 (Citron [6]).—Splenectomy was performed on a man, aged 38, with congenital hemolytic jaundice, with the result that the jaundice disappeared shortly after the operation. Six months later he became weak, subicteric and anemic; the hemoglobin fell to 65 per cent, and the liver became enlarged.

CASE 2 (Roth [7]).—A man, aged 31, had congenital hemolytic jaundice. There was a perfect result after operation. True hemolytic attacks occurred three and again five years after operation. Except for these attacks, the patient was perfectly well and was not jaundiced.

CASE 3 (Oehlecker [8]).—There was a perfect result after operation in this case. Two years later a hemolytic crisis occurred. The author suggested the influence of cold weather on the recurrence.

CASE 4 (Losio [9]).—The patient was a woman 22 years of age. A perfect result obtained after operation. Four months later there was a recurrence of jaundice.

CASE 5 (Gerhardt [10]).—The patient was a man 38 years of age. His symptoms were those of a typical case of hemolytic icterus. The spleen and liver were enlarged. The fragility was increased; the hemoglobin was 30 per cent. The urinary bilirubin was negative; the urobilin, positive. The urobilin was very much increased in the stools. After splenectomy, the jaundice disappeared almost completely. One and one-half months after operation, the patient had symptoms of obstructive jaundice. The feces were clay-colored. In the urine the reaction for bile was strongly positive, and that for urobilin faintly positive. Two months later the jaundice disappeared, the hemoglobin was 60 per cent, and the red blood count was 4,000,000. After one and one-half years, severe jaundice of an obstructive type recurred. Again in the urine the reaction for bile was positive, and that for urobilin, negative. A few days later the jaundice disappeared completely. This case of Gerhardt's is of special interest because of the similarity to one of the cases reported in this paper.

CASE 6 (Kaznelson [11]).—A woman, aged 58, had symptoms typical of hemolytic icterus; her condition grew worse after operation, and she died four months later. The author expressed the belief that hemolysis had continued, especially in the lungs, because the bilirubin content of the blood in the left auricle was higher than in other locations.

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6. Citron, Julius: Ueber einen Fall von Rezidiv eines haemolytischen Ikterus nach Milzexstirpation, Deutsche med. Wchnschr. **48**:79 (Jan. 12) 1922.

7. Roth, O.: Wiederauftreten von haemolytischen Anfall bei einem splenektomierten Fall von haemolytischen Ikterus, Folia haemat. **35**:1, 1928.

8. Oehlecker: Diskussion zu Sauer über Splenektomien beim congenitalen Haemolytischen Ikterus, Zentralbl. f. Chir. **47**:594 (Jan. 12) 1920.

9. Losio, Livio: A proposito di un caso singulere di ittero emolitico splenomegalico operato di splenectomia, Policlinico (sez. med.) **26**:410, 1919.

10. Gerhardt, D.: Beitrag zur lehre vom haemolytischen Ikterus, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **31**:644, 1918-1919.

11. Kaznelson, Paul: Erfahrungen über die Indicationen der Splenektomie und über deren Wirkungsmechanismus, Wien. Arch. f. inn. Med. **6**:87, 1924.

From this survey of the literature it is clear that the striking results of splenectomy in congenital and acquired hemolytic jaundice are not as constant as the general opinion would indicate.

We have observed two cases within the last few years in which splenectomy was unsuccessful. In one case the hemolytic anemia was not arrested by the operation, and was responsible for the death of the patient; in the second case, severe jaundice and anemia were, to say the least, an important contributory cause of the fatal issue.

REPORT OF CASES

CASE 1.—*History.*—I. L., a white schoolboy, aged 10 years, was admitted to the pediatric service of Mount Sinai Hospital on April 2, 1929. The family history was unimportant. He was born at term and developed normally. He had had measles, mumps and varicella. Two months before admission he had had abdominal pains, and for the past five weeks he had been markedly jaundiced. However, his mother definitely stated that the child always had been slightly yellow in the eyes, but that this had not attracted particular attention.

Physical Examination.—The patient was a well developed, afebrile boy of 10 years with marked icterus of the skin and sclerae. There was a slight systolic murmur at the apex of the heart. The lungs were clear. The liver and spleen were not palpable. No other physical findings of importance were present.

Laboratory Findings.—Examination of the blood showed: hemoglobin, 42 per cent; red cells, 1,930,000; white cells, 12,000; leukocytes, 87 per cent; lymphocytes, 13 per cent, and reticulated red cells, 6 per cent; anisocytosis, poikilocytosis and microcytosis were present. The fragility test showed an initial hemolysis at 0.88, and a complete hemolysis at 0.36. The platelet count was 115,000. The urine was negative for albumin and sugar. There were traces of bilirubin, and the urobilin was 85 mg. Leucine and tyrosine were not present. In the stool there was 3.29 mg. of urobilin daily. The urea nitrogen of the blood was 26 mg.; cholesterol, 224 mg. per hundred cubic centimeters; the direct van den Bergh reaction was delayed positive; the indirect reaction, 1:40,000. The icteric index was 55. The liver function, according to Rosenthal, was normal. Ewald's test meal showed normal values.

Clinical Course.—Subjectively, the child had no complaints. The icterus and the anemia continued with slight variations. The hemoglobin and red blood cell count rose slightly after transfusions of 350 cc. of citrated blood. He received Wilson's liver extract daily in amounts corresponding to 100 Gm. of liver. His spleen became just palpable.

During the patient's stay in the hospital, his relatives were examined. The father had a normal blood count and normal fragility of the red blood cells. His mother had normal values of hemoglobin and of red blood cells but somewhat increased fragility, the hemolysis starting at 0.52 of sodium chloride. The brother's blood gave normal figures and fragility, but he had an enlarged liver and constant urobilin in the urine.

The patient was discharged on May 21, without a change in his condition and with the diagnosis of congenital hemolytic icterus. He was advised to go to the country and to return for splenectomy after his physical condition had improved. He was readmitted on September 29, still jaundiced, with the spleen palpable one fingerbreadth below the costal margin.

On the second admission laboratory examination of the blood showed: hemoglobin, 40 per cent; red cells, 1,500,000; color index, 1.3; white cells, 13,400; neutrophilic polymorphonuclear leukocytes, 45.5 per cent; eosinophils, 3.5 per cent; basophils, 1.5 per cent; lymphocytes, 47.5 per cent; monocytes, 2 per cent, and reticulated red cells, 27 per cent; marked microcytosis, anisocytosis and poikilocytosis were present. The fragility of the red blood cells was: hemolysis started at 0.72, and was complete at 0.36. In the urine, the reaction for albumin and sugar was negative; for bilirubin, negative, and for urobilin, 3 plus. The direct van den Bergh reaction was negative; the indirect reaction, 1: 20,000.

Because of the progressive anemia splenectomy was performed on October 7 by Dr. R. Lewisohn. The spleen was enlarged; it was brought out without difficulty and removed in a typical manner. The only difficulty was that the pancreas reached to the hilus and had to be dissected carefully before clamps could be applied to the vessels. Transfusion was performed after the splenectomy. The splenic blood gave a reaction of 1: 8,300 to the indirect van den Bergh test, and a negative reaction to the direct test.

The postoperative course was uneventful except for an episode of pain in the left side and distention followed by a rise in temperature which lasted four days. The jaundice became less marked, but the child remained anemic. The number of nucleated red blood cells rose steadily, reaching the figure of 92 per hundred white cells. He was given another transfusion without improvement. An abscess developed on the face and on the right great toe. Although his condition was not satisfactory, he was discharged in the hope that he might improve at home. He remained there and was better for a week. Then he began to be constantly nauseated, complained of para-umbilical pains and vomited often. The temperature varied from 100 to 103 F. The jaundice did not clear, and puffiness developed around the eyes. The patient was readmitted to the hospital for the third time on December 13, five weeks after the splenectomy. He was acutely ill, markedly jaundiced and slightly dyspneic, but alert and responsive. There was a systolic murmur at the apex of the heart. The lungs were normal. The abdomen was soft. The edge of the liver was palpable 5 cm. below the costal margin and was tender. Several hemorrhages were seen in the fundus, and there was slight blurring of the disks. The child continued to have a fever, and attacks of para-umbilical pain recurred at irregular intervals with such intensity that an exploratory laparotomy was considered because of the possibility of an abscess of the liver. Because of other explanations to account for the pain, such as portal thrombosis or mere stretching of the Glisson's capsule due to the rapid enlargement of the liver, and because of the poor condition of the child, operation was not performed. The fever continued, and the anemia increased. The hemoglobin dropped to 20 per cent, and the red blood count to 1,000,000. The reaction for urobilin in the urine was strongly positive; 640 mg. daily was excreted in the stools. The icteric index rose to 77. The patient was given transfusion without improvement. Finally, pneumonia developed at the base of the right lung, and the patient died, three months after the splenectomy.

Autopsy.—At autopsy, the most conspicuous feature was enormous engorgement of the liver, which on histologic examination proved to be the result of active hyperemia (congestion of the periphery and not of the center of the lobules). This active hyperemia could also be seen in the removed spleen and in one of the accessory spleens removed at autopsy, as evidenced by enormous engorgement of the pulp and a relative absence of blood in the sinuses. The lymph nodes showed extensive extramedullary blood formation, with a predominance of erythropoiesis. The origin of the proerythroblasts could only be regarded as developing from

reticulum cells or pericytes. Marked hemolysis must have occurred, as was evidenced by striking iron pigmentation of the kidneys and hemoglobin in the renal epithelium. A small area of necrosis and calcification at the tip of the pancreas was found. It was regarded as a result of anemia due to ligature of a vessel and was not considered as of importance in causing death. The autopsy did not give any clue to explain why this case differed from other cases in which splenectomy was successful.

Histology of the Spleen.—The malpighian corpuscles were large with conspicuous secondary follicles. The pulp was enormously congested. The Schweigger-Seidel ellipsoids were numerous and readily recognized within the congested pulp. Owing to the excessive hyperemia of the pulp, the sinuses appeared compressed and bloodless. The lining cells were large and conspicuous. There was no evidence of erythrophagocytosis or iron pigment.

CASE 2.—*History.*—S. M., a white schoolgirl, aged 11 years, was admitted to the pediatric service of Mount Sinai Hospital on July 1, 1927. The parents were living and well. A maternal uncle had died after an operation for liver cirrhosis. The patient was the third child, born at full term; she had developed normally. She had had measles, mumps, whooping cough and German measles. Since 5 years of age she had been coughing continuously, occasionally with much expectoration. Periodically, she had attacks of exophthalmos lasting for a few days. Simultaneously, she had palpitation of the heart, but did not sweat intensely. Ten months prior to admission, she became jaundiced and remained so for four or five months. Three months prior to admission, the icterus recurred and continued, varying in intensity, up to the time of admission.

Physical Examination.—The patient was a fairly well developed child with jaundice; no petechiae were seen. There was exophthalmos. The teeth were defective; the tonsils were small; the thyroid isthmus was enlarged. The chest was symmetrical; the hilus dulness was increased. Throughout the chest, especially at the base, very coarse dry râles and sibilant rhonchi were heard. The borders of the heart were widened to the right and left. The pulse was regular, 140 beats per minute. High-pitched systolic murmurs were heard all over the heart, transmitted to the axilla. The abdomen was somewhat prominent; the liver was not enlarged. The lower pole of the spleen was felt 1 cm. below the umbilicus, the mesial border extending 1 cm. to the right of the umbilicus. The finger-nails were "watch crystal nails." The toes showed a tendency to clubbing. The hands were warm and moist and showed slight tremor.

Laboratory Findings.—Examination of the blood showed: hemoglobin, 32 per cent; red cells, 1,730,000; white cells, 7,400, with a normal differential count; poikilocytosis and anisocytosis; reticulated red cells, 6 per cent; platelets, 70,000. The fragility of the red blood cells was: hemolysis started at over 0.50, and was complete at 0.32. In the urine, the reaction for albumin was positive; for sugar, negative; for urobilin, positive, and for bile, negative. Six hundred milligrams of urobilin was excreted in the stools daily. The Wassermann reaction of the blood was negative; the direct van den Bergh reaction was delayed positive; the indirect reaction, 1 : 30,000.

Roentgen examination of the long bones and the skull showed them to be normal; the chest did not show definite abnormality. The basal metabolism was +24. An electrocardiogram showed a simple tachycardia. A second roentgen examination of the chest revealed a honeycomb-like shadow at the left cardiophrenic angle, probably a chronic pneumonic process. Examination of the blood of the parents gave negative results. The diagnosis was acquired hemolytic jaundice,

chronic pneumonia and exophthalmic goiter. The child was given a transfusion of 500 cc. of citrated blood and was discharged from the hospital.

After she left the hospital, she did very well. The hemoglobin increased to 70 per cent. She attended school. Slowly, dyspnea on exertion developed; the jaundice, which had been very much improved, now increased, and the exophthalmos was more marked in the last week before her second admission. She was readmitted to the hospital on Feb. 21, 1928, seven months after her discharge.

On admission, the patient's face was puffy and slightly icteric; she appeared chronically ill, but comfortable, happy and exceedingly bright. There were a few petechiae on the skin and in the right conjunctiva. The exophthalmos was marked; the thyroid gland was palpable. The heart was enlarged and had a loud systolic murmur. The lungs presented a slight dulness anteriorly on the left and posteriorly on the right, with diminished breath sounds and scattered musical and many bubbling râles. The spleen was hard and regular, 4 cm. below the umbilical level. The liver was 3 cm. above the umbilicus. The patient had clubbing of the fingers, cyanosis of the nails and slight tremor.

Laboratory Findings.—Examination of the blood showed: hemoglobin, 18 per cent; red blood cells, 680,000; white cells, 6,000; neutrophilic polymorphonuclear leukocytes, 69 per cent; eosinophils, 1 per cent; basophils, 2 per cent; lymphocytes, 25 per cent; myelocytes, 4 per cent. The fragility of the red cells started at 0.60, and was complete at 0.34 of sodium chloride. In the urine, the reaction for bile was negative; that for urobilin, positive. After a transfusion, the hemoblogin rose to 41 per cent, and reticulated red blood cells to 12.5 per cent. The patient was operated on by Dr. A. A. Berg on March 10. A large, firm, dark plum-colored spleen was removed. No accessory spleens were seen.

Histology of the Spleen.—The malpighian corpuscles of the spleen were generally small, composed exclusively of small lymphocytes. Within the perifollicular zone as well as throughout the entire pulp there was seen a striking engorgement with blood. The meshes of the pulp reticulum were filled with erythrocytes. The venous sinuses, however, stood out conspicuously because they were far more separated by wide pulp cords than in a normal spleen, and because they contained far less red blood cells than the surrounding pulp meshwork. The endothelial cells lining the sinuses were large and conspicuous. Among the cells that populated the splenic reticulum there were in addition to the erythrocytes, lymphocytes and polymorphonuclear leukocytes. There were also plasma cells, scattered and in small groups, occasional eosinophil myelocytes, but rarely macrophages, which contained red blood cells or blood pigment. A sporadic multinucleated giant cell could be found within a sinus. The vascular ramifications did not show any changes.

Clinical Course.—Immediately after the operation, the blood bilirubin was 4.5 mg. (Kuttner method), with an icteric index of 1.2; the splenic blood bilirubin was 24 mg. (Kuttner method), with an icteric index of 60. The day following operation, the condition of the child was very good; the jaundice had almost entirely disappeared, and the sclerae were subicteric. During the next days pneumonia developed, the temperature rose to over 103 F., and the course was rather stormy. The urine showed albumin, red blood cells and casts; they disappeared gradually. The patient left the hospital in a very much improved condition on May 15.

She was readmitted on Jan. 16, 1929. The child had done splendidly up to one week prior to admission, when she began to cough and had a sore throat and fever of 104 F. Two days before admission to the hospital, jaundice had developed and became rapidly deeper than it had ever been before. The stools had been light

brown, but not completely white at any time. She was acutely ill, deeply jaundiced and dyspneic. The exophthalmos was striking. Cough was present; the sputum was tenacious but not foul-smelling. The temperature was 101 F. The heart was enlarged; the heart sounds were so booming that the murmur could not be distinctly heard. The lungs showed evidence of infiltration of the left base and transmitted signs to the right. The liver was enlarged, and the epigastrium tender. There was no edema. Tremor of the fingers was present. The hemoglobin was 30 per cent, the red blood count 1,650,000, the white blood count 19,300, the neutrophilic polymorphonuclears 84 per cent and the lymphocytes 16 per cent. The patient now presented symptoms of an obstructive jaundice. The urine showed 4 plus bile and a trace of urobilin. The direct van den Bergh reaction was promptly positive; the indirect reaction, 1 : 33,000. The stool was light brown; it contained a trace of bile, and the reaction for urobilin was positive. The patient was practically afebrile, but the course was steadily downhill, with increasing jaundice. She presented a striking triad of severe jaundice, exophthalmic goiter and bronchiectasis with pneumonia. She died three days after admission, nine months after operation, because of heart failure.

Autopsy.—Necropsy revealed an acute fibrinous pleuritis of both lungs. The bronchi of both lower lobes showed marked spindle-shaped dilatation and were filled with thick, creamy, greenish pus. There was an area of bronchopneumonia in the right upper lobe. The heart muscle showed striking fatty infiltration. The liver weighed 1,100 Gm. and was of a dark coffee-brown color. The gallbladder was filled with a dark, very viscid and tenacious bile. The cystic duct contained a few small concrements. The common duct was pressed on by a walnut-sized lymph gland in the porta hepatis. Bile was expressed from the gallbladder only with difficulty. The kidneys were deeply bile-stained. The small and large intestines contained yellowish-green material. The bronchial, mesenteric and peripancreatic lymph nodes were markedly enlarged. The thyroid gland was large and lobular; on section, it contained a small amount of colloid.

Histologic examination of the bronchiectasis showed squamous cell metaplasia of the epithelium, which was in places destroyed by an acute purulent inflammation of the wall. The smooth muscle and elastic fibers were destroyed by the diffuse purulent infiltration of the wall.

The liver showed very marked hyperemia of the capillaries, especially of the peripheral zones of the lobules. There was round cell infiltration of the periportal spaces. There was much iron pigment in the Kupffer cells; less was found within the liver cells, which contained, however, much bile pigment.

The thyroid showed epithelial hyperplasia; the acini were lined by high columnar epithelium, which was thrown up in folds. There was no lymphocytic infiltration of the stroma. The acini contained some colloid. The lymph nodes showed large follicles with large germinal centers. The sinuses contained many mononuclear cells (histiocytes), which frequently showed erythrophagocytosis.

COMMENT

The clinical features and laboratory findings in both cases speak in favor of the diagnosis of hemolytic jaundice.

It is justifiable to consider the first case as one of the congenital type, because the patient was slightly icteric all his life, because he showed microcytosis of the red blood cells and also because of the increased

fragility of the erythrocytes found in the mother and the constant urobilinuria of the brother.

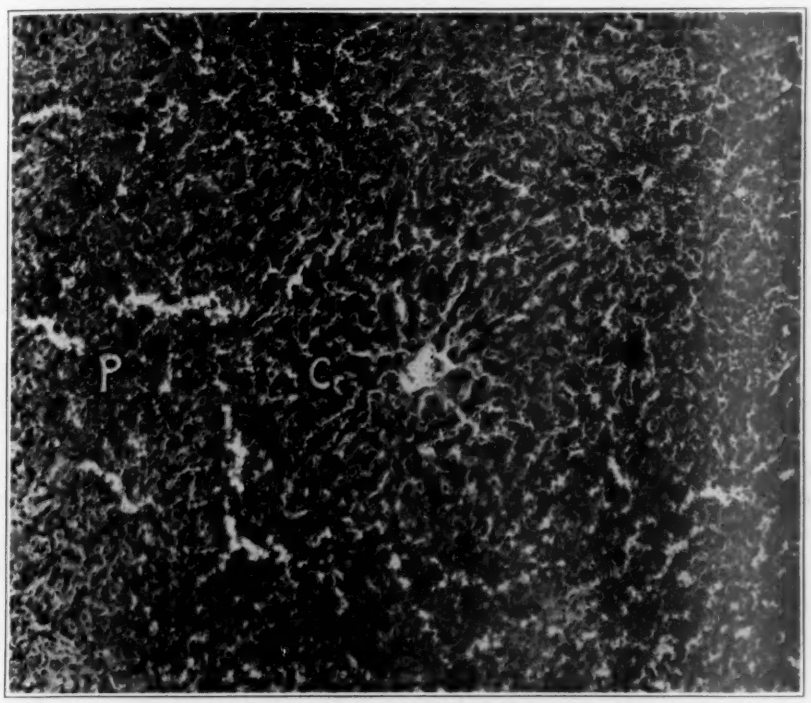
Splenectomy was indicated because of the severe anemia, which was not relieved by conservative medical treatment and transfusions. There was no contraindication, and prompt recovery was to be expected after the uneventful operation. The responsibility of the spleen for the hemolytic condition was evident from the high bilirubin content of the splenic blood, which by far exceeded that of the general circulation. The histologic picture of the spleen—excessive engorgement of the pulp and relative anemia of the sinus—was that usually seen in hemolytic jaundice and confirmed the clinical diagnosis. The anatomic observations at necropsy were dominated by the severe secondary anemia with foci of extramedullary blood formation in the lymph nodes and liver, an occurrence commonly seen only in excessive anemia, when the bone marrow is unable to cope with the demands for blood regeneration. The striking erythrophagocytosis seen in the lymph nodes and liver and the vast iron pigmentation of Kupffer cells and tubular epithelium of the kidneys prove that the blood destruction had continued in spite of the removal of the spleen. If one accepts the opinion that hemolytic jaundice is due to an overfunction of the spleen as part of the reticulo-endothelial system, one recognizes that the remaining portion of that apparatus so widely distributed over the entire body may well take up and continue the exaggerated blood destruction.

Because the examination of the blood of the parents of the second patient did not reveal any evidence of a hemolytic process and because of the long-standing pulmonary infection, the second case was considered as an acquired hemolytic icterus. The histologic picture of the spleen in this case was also characteristic of hemolytic jaundice because of the excessive engorgement of the meshes of the pulp with erythrocytes and the collapse of the sinus. There was conspicuous erythrophagocytosis by the splenic macrophages mainly within the marginal zones around the malpighian corpuscles.

The result of the splenectomy in this case was striking, and the patient remained perfectly well for nine months when she had a severe relapse of the pulmonary disease. Then icterus recurred more intensively than ever before. The puzzling feature of the terminal phase of her disease was the fact that the jaundice was now of an obstructive nature (light-colored stools, bilirubinuria, only traces of urobilin and a prompt positive direct van den Bergh reaction).

Necropsy revealed a chronic bronchiectasis of the lower lobe of the right lung with acute purulent bronchitis with subsequent ulcerations of the bronchial wall, peribronchitis and pneumonia. Not only the bronchial but also the abdominal lymph nodes showed marked inflam-

matory swelling, an occurrence frequently observed in cases of pulmonary infections, particularly in children. There were enlarged lymph nodes in the hilus of the liver which surrounded the common duct. The bile of the gallbladder and of the large bile ducts was very dark and extremely viscid. This fact, in conjunction with the compression of the common duct by the swollen hilar lymph nodes, was responsible for the interference with the biliary outflow and accounted for the terminal obstructive icterus. That both factors were equally important in the



Section of the liver in case 1, showing conspicuous hyperemia in the periphery (*P*) of the lobule but normal circulatory conditions within the center (*C*).

production of the icterus is evident because in other observations of hilar lymphadenitis in cases of systemic infections in which there was no alteration of the consistence of the bile, icterus was not present. In this case the anemia was striking on the last admission. The increased pigmentation of the bile, together with the histologic observations, of marked erythrophagocytosis in the lymph nodes and liver and iron pigmentation of the Kupffer cells and liver parenchyma, proves the recurrence of a severe hemolytic process which had only temporarily been arrested by the splenectomy nine months prior to death.

Retrospectively, one must question the advisability of the splenectomy in this case. Contrary to other cases of acquired hemolytic jaundice in which icterus followed an acute infectious disease, there existed in this patient a progressive chronic pulmonary infection. It seems rational to think that by removal of the spleen the body was deprived of an organ most important in the combating of infection, and that the severe systemic consequences of the recurrent pulmonary suppuration can be related to this weakening of the defense.

The reason for the hyperfunction of the spleen in congenital hemolytic jaundice has not yet been ascertained. It may be well to call attention to a striking histologic feature that was observed in the liver in both cases. The sinusoids in the peripheral portions of the lobules were enormously dilated and engorged; the center, however, was normal. This picture is just the reverse of that regularly found in passive congestion, in which the centro-acinar capillaries are distended and the peripheral sinusoids are normal. This situation deserves attention because it is analogous to the type of splenic hyperemia in hemolytic jaundice. Here the pulp shows only engorgement and the sinuses are empty. This contrasts with the findings in passive congestion due to general or local causes in which the sinuses are enormously congested; the meshes of the pulp, however, are not overfilled with blood. This difference in the histologic picture indicates a difference in the mechanism, and therefore Menetrier and Gauckler have referred to the splenic engorgement of the hemolytic jaundice as active hyperemia. The picture of hepatic hyperemia in the cases here reported, contrasting so strikingly with ordinary passive congestion, indicates an identical active mechanism, which might be of some significance in the pathogenesis.

SUMMARY AND CONCLUSIONS

1. Two cases of hemolytic jaundice are reported, one of the acquired, the other of the congenital, type.

2. Both patients were subjected to splenectomy with poor results.

3. In the case of congenital hemolytic jaundice, death was due to the persistence of the hemolysis in spite of splenectomy.

4. In the acquired type, splenectomy had been performed in the presence of a chronic infection. This may have had some depressing effect on defense mechanism against infection. Further studies should be made to ascertain whether or not chronic infection occurring in a case of hemolytic jaundice should be considered a contraindication to splenectomy.

5. Active hyperemia was found in both the spleen and the liver. This should also be studied further in connection with the possible mechanism of the pathogenesis of hemolytic jaundice.

SUPRARENAL TUMOR WITH METASTASES*

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The case reported in this paper was one of Hutchinson's tumor of the left suprarenal medulla with metastases to the skull and sacrum.

History.—A boy, aged 3 years, was admitted to the hospital in January, with the complaint of paralysis of the face and a tumor in the abdomen. The family history was unimportant. It was noted that the child had never been in good health, had not eaten or gained weight normally, and had never slept soundly; the appetite had been poor during the last four or five months.

In the November preceding hospitalization there had been a severe gastro-intestinal upset, with nausea and vomiting for two days; obstinate constipation had persisted for a week. Two days later, the child burned his lip with hot cereal,

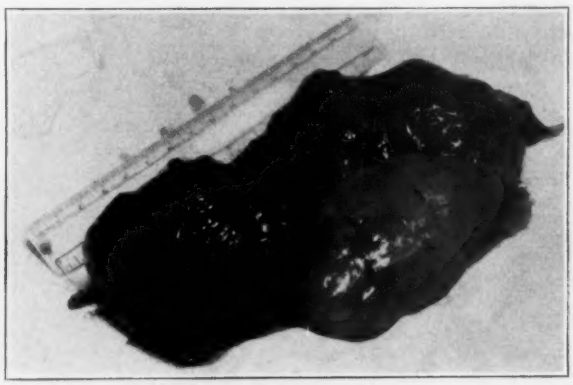

Fig. 1.—Photograph of the tumor with the kidney shelled out of mass. Part of the suprarenal cortex may be seen on the left.

and the mother first noticed paralysis of the left side of the face. Shortly after this, there was considerable edema of the right side of the face, and the patient complained of pain in the cheek, particularly when he was moving his jaw. Following this, the appetite was fair, and the patient was able to eat until December 25, when he refused everything but liquids. A physician was called, who suggested that the tonsils were infected. They were removed on January 2, and for many days the child was unable to swallow well, taking only liquids. Consequently, there was considerable loss of weight, and the bowels were constipated in spite of active catharsis and daily enemas. In the two weeks prior to admission, the patient vomited practically everything taken. He had black, sticky, tarry stools, and frequency and dysuria.

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* From the Milwaukee Children's Hospital and the Department of Pediatrics of the Marquette University School of Medicine.

Examination.—Examination revealed a very poorly nourished, dehydrated white boy with a left-sided facial paralysis. The pupils were unequal, the right slightly contracted and reacting sluggishly. There was a slight nystagmus to the left. There was some paralysis of the left half of the tongue, which did not respond to stimulation. There was slight rigidity of the neck and apparent pain on flexion. A large tumor mass could be palpated filling the left upper and middle areas of the abdomen, and centering about the left kidney region. The mass was irregular,

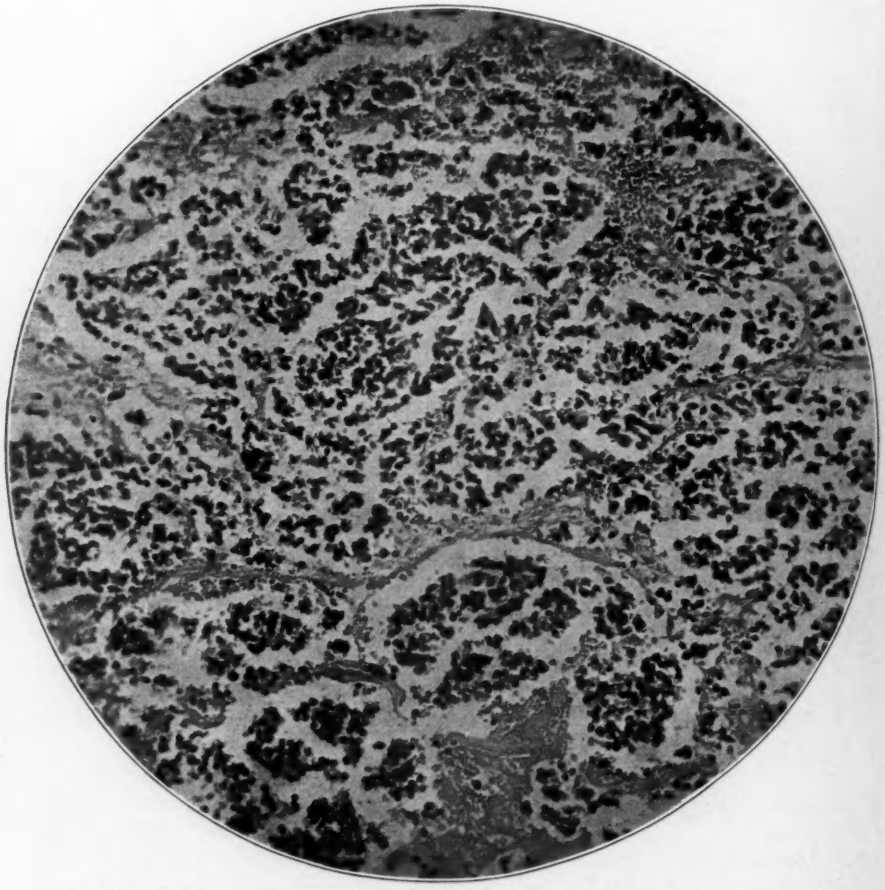

Fig. 2.—Photomicrograph of a section of the tumor, showing acinar structure; low power magnification.

hard, apparently attached to the posterior abdominal wall, and about 25 cm., or 10 inches, in diameter.

A clinical diagnosis was made of left suprarenal tumor with metastases to the skull. The patient died eleven hours after admission.

Autopsy.—Postmortem examination revealed moderate edema of the brain with an area of hemorrhage 2 by 1.5 cm. in the left cerebellum. Surrounding the hemorrhage was an area of soft friable brain tissue, a metastasis. There was also

a metastasis in the petrous portion of the temporal bone, measuring 4 by 2.5 cm. and extending into the bone. In the abdomen, there was a mass in the left kidney region measuring 20 by 15 by 5 cm., which was retroperitoneal but had involved several coils of the small intestine in a mass of adhesions. This tumor mass was dark red and mottled, with brownish and greenish discolorations. It weighed 500 Gm. and contained areas of cystic degeneration. The kidney could easily be separated from the mass; it weighed 85 Gm., and showed hydronephrosis

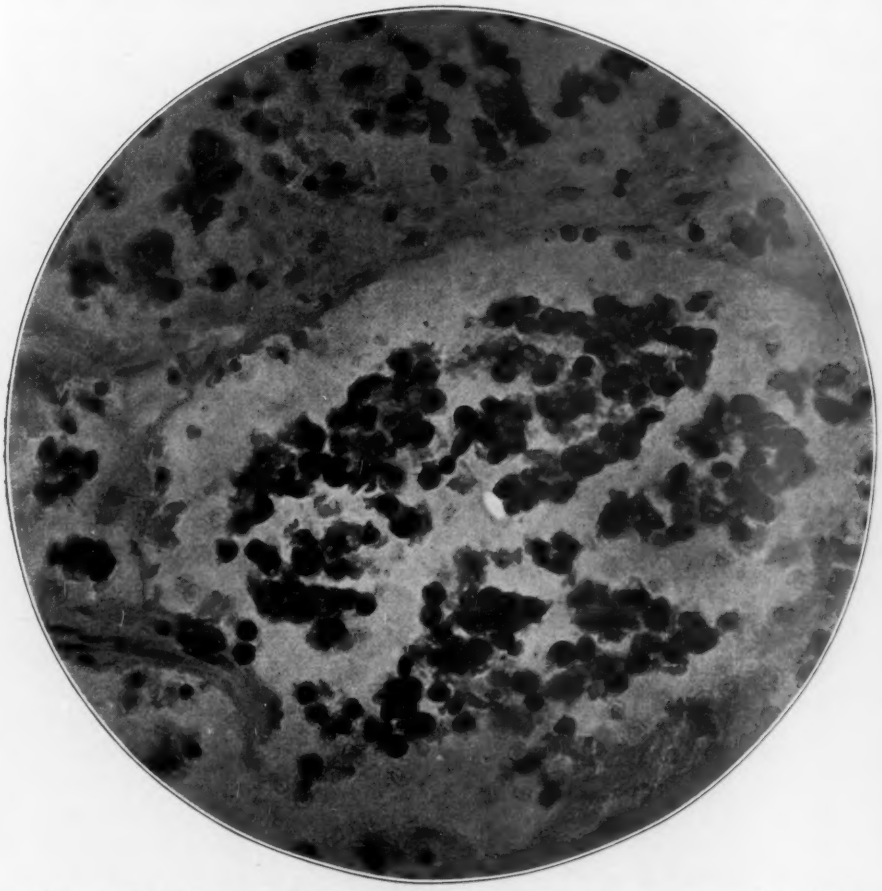

Fig. 3.—Photomicrograph showing neurocytoma cells; high power magnification.

and fatty degeneration. The cortex of the left suprarenal gland was found spread around the tumor. There was a metastasis 3.5 by 2.5 cm. in the middle of the sacrum behind the bladder. The mesenteric, lumbar and postmediastinal glands were not involved. The blood culture showed pneumococci. Death was attributed to pneumococcus septicemia. The anatomic diagnosis was tumor of the left suprarenal gland with metastases to the sacrum and skull.

Microscopic studies of sections of the tumor revealed a variegated architecture, but mostly an infiltration of small, round, sarcoma-like cells which were diagnosed

as neurocytoma. The metastases showed the same picture (confirmed by Dr. O. T. Schulze, Chicago).

COMMENT

Tumors of the type found in the case reported originate from the medulla, and thus do not produce the symptoms associated with involvement of the suprarenal cortex. Tumors of the left suprarenal medulla usually produce vague, indefinite symptoms at the onset and do not direct attention to the abdomen until the tumor produces obstruction or irritation. The tumor in the case reported, however, produced the first observed symptoms in the gastro-intestinal tract, with nausea, vomiting and constipation. The second symptoms were produced by the metastases in the brain. Tumors of the right suprarenal gland usually produce abdominal pain, and thus direct attention to their presence. The diagnosis of Hutchinson's tumor (neurocytoma, hypernephroma or medulloblastoma) with metastases has been made in three cases in the Milwaukee Children's Hospital during the past five years. This is the first case to come to necropsy. A review of the literature and a description of the syndrome may be found in Griffith and Mitchell's and in Garrod's textbooks.

ACUTE EPIDURAL ABSCESS OF THE SPINAL CANAL OF PROBABLE METASTATIC ORIGIN *

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In 1926, Dandy [1] reviewed the literature and collected twenty-six cases of acute epidural abscess. One other case has been reported since then by Smitt.[2] Prior to Dandy's paper, two other cases were reported by Mixter [3] and Spiller and Wright,[4] which he did not include in his report. These cases are mentioned because their reports are easily available and because their cases are somewhat similar to our own. None of these patients was under 15 years of age.

In 1926, Woltman and Adson [5] reviewed the literature and collected twenty-nine cases of abscess of the spinal cord, and reported one case of their own. Since then Bennett and Keegan [6] have reported another case. Four of these patients were under 10 years of age.

Clinically, the two conditions are quite similar, both presenting the signs and symptoms of an acute infection together with neurologic findings varying from localized pain and partial paralysis, spastic in type, to complete transverse myelitis. Operation is the treatment of choice, and it would seem that epidural abscess should be more amenable to treatment than abscesses of the cord. However, only two recoveries

* Submitted for publication, June 8, 1931.

* From the Children's Department, Wesley Hospital.

1. Dandy, Walter E.: Abscesses and Inflammatory Tumors in the Spinal Epidural Space (So-Called Pachymeningitis Externa), Arch. Surg. **13**:477 (Oct.) 1926.

2. Smitt, W. G. S.: Epidural Spinal Abscess, Rev. neurol. **36**:512 (Nov.) 1929.

3. Mixter, W. J.: A Case of Epidural Intraspinal Abscess of Pyogenic Origin, Boston M. & S. J. **175**:864, 1916.

4. Spiller, W. G., and Wright, W. M.: Extradural Abscess of the Midthoracic Region of the Spinal Canal Secondary to a Boil of the Neck, Arch. Neurol. & Psychiat. **5**:107 (Jan.) 1921.

5. Woltman, H. W., and Adson, A. W.: Abscess of the Spinal Cord: Report of a Case with Functional Recovery Following Operation, Brain **49**: 193 (July) 1926.

6. Bennett, A. E., and Keegan, J. J.: Subdural Abscess with Functional Recovery Following Operation, Arch. Neurol. & Psychiat. **10**:329 (Feb.) 1928.

from the former and three from the latter condition have been reported out of an approximately equal number of cases. Unfortunately, a diagnosis has rarely been made before operation or even ante mortem.

In seventeen of the cases collected by Dandy the abscesses were metastatic in origin, but in only a part of these cases was the source of the infection given (furuncles, phlebitis). The anatomy of the epidural space has been worked out by Dandy and is here restated in part.

> Dissection of the cadaver shows that the spinal epidural space is present only dorsal to the spinal nerve attachments. Ventral to the nerves the dura is everywhere closely applied to the bones of the vertebrae and their ligaments from the first cervical to the second sacral vertebra. Below the second sacral bony segment the epidural space surrounds the dura on all sides. The epidural space is filled with fat and loose areolar tissue containing numerous veins. . . . Of greatest importance are the variations in size of the epidural space. In the cervical region the space is only potential there being only a few strands of fibrous tissue and almost no fat between the laminae and dura. The epidural space really begins to appear at the seventh cervical vertebra and gradually deepens along the thoracic vertebrae attaining a depth of about 0.5 to 0.75 cm. between the fourth and the eighth dorsal vertebrae. The space tapers again and becomes shallow between the eleventh thoracic and second lumbar vertebrae. Over the remaining lumbar and the first and second sacral vertebrae the epidural space attains its greatest depth. At the second sacral vertebra the dural envelope ends and a continuation of the epidural tissue fills the caudal end of the sacral canal. . . . The spinal epidural space is therefore filled with tissues—fat and loose areolar—which offer a foothold for current hematogenous infections, and the intraspinous location of these tissues makes trauma an important inciting agent in the development of hematogenous infections.

REPORT OF CASE

History.—O. C., a white girl, 14 years of age, was admitted to the hospital, on May 9, 1931, with a chief complaint of inability to use her legs. The family history bore no relation to the present illness. The patient was a normal full term baby, weighing 8½ pounds (3,855 Gm.). She was breast fed for fourteen months and developed normally. She had measles, mumps, whooping cough, chickenpox and frequent sore throats. Three months before admission to the hospital the patient had seven boils on her face. Three weeks before admission she had a chill, fever, headache and general aching and had been acutely ill for two or three days. Following this she was able to get up and be about, but the mother though that she still had some fever. Two weeks later she began to complain of numbness and tingling in both legs with an occasional sharp pain that varied in its location. This lasted for two days. When she awoke on the third morning she was unable to use her legs. For the next week she remained at home in bed. She had fever during this time, and because she was unable to void she had to be catheterized at intervals.

Examination.—On admission to the hospital the patient's temperature was 100.2 F. She was a fairly well nourished and developed girl. The skin was clear, except for a few blisters on the right side, which her mother said were caused by a hot water bottle the night before, and a decubitus on the right hip.

The pupils reacted equally to light and in accommodation. The gums were clean and there were no carious teeth. The tonsils were small and not injected. The cervical glands were not enlarged. The chest was symmetrical; the lungs were clear; the heart rate was 104 and the rhythm regular; no murmurs and no enlargement were noted. The abdomen was full but not definitely distended. There was slight tenderness on deep pressure. The liver and spleen were not palpable. The bladder was moderately distended.

No abnormality was detected in any of the cranial nerves. The patient was unable to move her legs. The abdominal reflexes were absent. There was a loss of deep and superficial reflexes in the lower extremities. In the upper extremities they were present and equal. There was a complete loss of all sensation below the fifth rib. Above this point there was an area of hyperesthesia.

The urine showed a small amount of albumin and a number of pus cells in clumps. The hemoglobin was 75 per cent, the white blood cells numbered 29,000 with 85 per cent polymorphonuclear leukocytes. The Wassermann test of the blood was negative.

Course.—A diagnosis of transverse myelitis following influenza was made. On lumbar puncture a few drops of thick yellow fluid which coagulated on standing were obtained. During the first twenty-four hours the temperature ranged between 100 and 104 F. We were unable to tell what part the apparent genitourinary infection played in the production of the fever and leukocytosis but thought it probably sufficient to produce them, and we were, therefore, not particularly worried about the possibility of infection elsewhere. Eighteen hours after admission the limit of the zone of anesthesia had extended up one spinal segment. Because the lesion of the spinal cord was apparently spreading, and because there was obviously a spinal block that we felt might be due to swelling of the cord itself, operation was decided on. This was done by Dr. A. L. Blesh twenty-four hours after admission. When the laminae and spinous process of the fifth dorsal vertebra were removed, a thick grayish-yellow pus exuded. The dura at this point was eroded, and a red swollen cord was visible beneath. The laminae of the sixth and seventh dorsal vertebrae were also removed, and thick pus lay between them and the dura. Drains were inserted and the wound closed. Following operation spinal fluid and pus drained freely from the incision.

The patient had a rather severe postoperative reaction, but the next day her temperature was lower, and there was no apparent progress of the paralysis upward. On May 11, however, a paralytic ileus developed which we were unable to control, and on the next day the patient died.

Necropsy.—Necropsy showed that the abscess extended from the third to the eighth dorsal vertebra. There were no abscesses in the cord. Examination of the brain was not permitted, but a postmortem cisternal puncture showed a normal fluid. No other abscesses were found.

COMMENT

It is interesting to note that the parents later remembered that the patient had received a rather severe blow on the back while playing basketball some time between the appearance of the boils on the face and the onset of the present illness. It is, of course, impossible to determine the exact cause of the epidural abscess, or to say whether or not the boils were in any way responsible. It seems probable, however, that the

organism entered the body by way of these infections in the skin, and that the blow on the back may have been responsible for the localization in the epidural space. This sequence of events is similar to that so often obtained in the histories of children with acute osteomyelitis, and suggests that it is well to bear in mind the possibility of epidural abscess in children.

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SUPRARENAL HEMORRHAGE IN THE NEW-BORN INFANT*

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Suprarenal hemorrhage in the new-born infant is a rather common condition, which, as a rule, is diagnosed only at autopsy. In a few instances the diagnosis was made in vivo, for instance by Corcoran and Strauss,[1] who operated on such a child for what they thought was an acute abdominal condition, and found to their surprise a hemorrhage of the suprarenal glands.

Goldzieher[2] described a definite syndrome on the basis of which suprarenal hemorrhage in the new-born infant can be diagnosed. Such cases diagnosed in vivo and confirmed at autopsy were reported by Goldzieher and Greenwald.[3] The main symptoms on which such a diagnosis can be made are rapid respiration and high temperature with normal lungs. The presence of a palpable mass in the abdomen is confirmatory evidence. Other symptoms that may be present are convulsions, rash on the skin, petechiae on the skin or mucous membranes, jaundice and abdominal symptoms.

A case observed at the Coney Island Hospital seems to bear out these contentions and appears to show all the characteristic features of the syndrome.

REPORT OF A CASE

History.—T., a girl, whose mother was a multipara, was born at the Coney Island Hospital on March 12, 1931. The mother showed evidence of toxemia on March 3, and was admitted to the hospital with symptoms of vomiting, headache, dizziness, spots before the eyes, edema and albuminuria. The blood pressure was 182 systolic and 128 diastolic. She was discharged from the hospital on March 10, on the disappearance of the toxic symptoms. On March 12, she went into labor. The duration of labor was about four hours, but the obstetrician had difficulty in delivering the shoulders of the infant, who was cyanotic and breathless. Artificial means of resuscitation were used, such as pressure on the lower ribs, mouth to mouth insufflation and immersion in hot and cold water. The

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* From the Pediatric Department of the Coney Island Hospital, Dr. Judson P. Pendleton, chief of service.

1. Corcoran, W. J., and Strauss, A. A.: Suprarenal Hemorrhage in the New-Born, J. A. M. A. **82**:626 (Feb. 23) 1924.

2. Goldzieher, M. A.: The Adrenals, New York, The Macmillan Company, 1929.

3. Goldzieher, M. A., and Greenwald, H. M.: Hemorrhage of the Suprarenals in a New-Born Infant: Diagnosis and Therapy, Am. J. Dis. Child. **36**:324 (Aug.) 1928.

infant began to breathe after five minutes, but remained cyanotic for about two hours. Results of the physical examination by the house physician at that time were reported as negative. On the following day, March 13, there was an elevation of temperature to 100 F., and hemorrhagic areas in both sclerae were noted. On March 14, the temperature was 102 F., and the nurse noticed slight twitchings on the right side lasting a few minutes. On March 15, the temperature was 105 F., respirations were rapid, and a diagnosis of pneumonia was made. The infant was seen by me on that day.

Examination.—Physical examination revealed an infant who appeared critically ill; the face was yellow with a circumoral cyanosis. The cry was weak, and the respirations were rapid and shallow, the rate varying from 120 to 170 per minute. The anterior fontanel was patent and depressed. The eyes showed hemorrhages in both sclerae. The mouth did not show any abnormalities. The neck was lax. The heart sounds were rapid and of poor quality, and there were no murmurs. The chest was normally resonant throughout, and the breath sounds were normal. The abdomen was slightly distended, but not rigid. In the left flank of the abdomen, an oval tumor mass about the size of an egg was palpable. It seemed to be in the region of the kidney, and was firm and freely movable. A diagnosis of suprarenal hemorrhage was made.

Chemical analysis of the blood revealed: urea nitrogen, 30 mg., creatinine, 2.3 mg., uric acid, 6.6 mg., and dextrose, 63 mg. in 100 cc. of blood. A roentgenogram of the chest showed a moderate enlargement of the heart in all diameters. The lung fields were clear. Twenty cubic centimeters of paternal blood was given intramuscularly.

Course.—On March 16, the fifth day of life, the temperature dropped to 101 F., and the general condition seemed somewhat improved. The mass in the left flank, however, remained unchanged in size. A purulent discharge from the right eye was noted, and a smear revealed gram-positive cocci in pairs and clumps. For the next four days the temperature fluctuated between 100 and 101 F., and the general condition continued to improve. On March 19, a hemorrhagic area was noted on the left side of the back. Chemical examination of the blood on March 20 revealed: urea nitrogen, 16.7 mg.; creatinine, 1.4 mg.; uric acid, 3 mg., and dextrose, 69 mg. in 100 cc. of blood. The temperature reached normal on March 22. The respirations, however, were still around 60 per minute. On March 16, the hemoglobin (Sahli) was 94 per cent. The red blood count was 5,130,000, and the white blood count, 13,000; the differential count was: polymorphonuclears, 60 per cent; small lymphocytes, 32 per cent, and monocytes, 8 per cent. The mother's and infant's Wassermann and Kahn reactions were negative. The bleeding time was one minute, and the coagulation time, five and one-half minutes. The birth weight of the infant was 10 pounds and 1 ounce (4.5 Kg.). The lowest point in the weight curve was reached on the fifth day of the infant's life, when it was 8 pounds and 15 ounces (4 Kg.). The infant was discharged on March 22, the eleventh day of life, weighing 9 pounds and 2 ounces (4.1 Kg.). The general condition was greatly improved, the temperature was normal, and respirations were about 60 per minute. The feeding consisted of nursing at the breast every three hours. The infant was observed weekly for the next few weeks, and a gradual reduction in size of the tumor mass was noticed. Four weeks after leaving the hospital there was no more evidence of a tumor mass in the abdomen. The infant showed normal progress.

COMMENT

Pathogenesis of suprarenal hemorrhage in the new-born infant is a much discussed question, with an extensive literature on the topic.

In a number of cases, the case reported belongs to this group, difficult labor has been reported or artificial respiration has been necessary for resuscitation. The trauma of birth or the handling in order to resuscitate the child may well account for the hemorrhage of the organ. The fine capillaries of the suprarenal gland are usually intensely congested post partum. Involution of the suprarenal gland sets in almost immediately after birth, and leaves the distended capillaries deprived of their protection by the surrounding tissue and thus exposed to rupture. The added birth trauma may well explain the hemorrhage into the suprarenal tissue.

Among the clinical symptoms observed, the outstanding ones are the rise in temperature and rapid respiration, which are so characteristic that such cases should be diagnosed provided there are no pulmonary changes present. As a matter of fact, many cases of suprarenal hemorrhage in the new-born infant have been clinically diagnosed as pneumonia. This happened in the case reported in this paper before the patient's admission to my service. These cardinal symptoms are apparently based on the deficiency in functions of the suprarenal cortex. The rôle of the cortex in heat production was asserted by Cramer,[4] Marine and Baumann[5] and others, while the regulation of respiration by the suprarenal cortex has been described by Bornstein,[6] Goldzieher, Kühl[7] and others.

A recent paper by Arnold,[8] in which he described four cases of suprarenal hemorrhage in the new-born infant, does not seem to bear out the Goldzieher syndrome, as his patients did not show any rise in temperature. In all his cases there was rupture into the abdominal cavity and a clinical picture of abdominal shock. I have recently observed a similar picture in a child 12 days old as a result of a ruptured hemorrhagic cyst of the liver. In Arnold's case 4, the only one in which the respiration was noted, he reported rapid shallow respiration. Thus, the contradiction narrows down to the absence of hyperpyrexia. In reviewing the literature, it can be stated that the clinical data of the cases reported, although as a rule very meager, frequentiy include hyperpyrexia. In a number of cases, besides those of Arnold, the absence of a rise in temperature can be noted. Thus it seems that a rise in temperature may not always be present, which is well in accord with the observations on physiologic experiments by Trendelenburg,[9]

4. Cramer, W.: Brit. J. Path. **7**:95 (June) 1926.
5. Marine, D., and Baumann, E. J.: Am. J. Physiol. **59**:353 (Feb.) 1922.
6. Bornstein, A., and Holm, K.: Ztschr. f. d. ges. exper. Med. **37**:1, 1923.
7. Kühl, G.: Pflüger's Arch. f. d. ges. Physiol. **215**:277 (Jan.) 1927.
8. Arnold, D. P.: Massive Suprarenal Hemorrhage in a New-Born Infant, Am. J. Dis. Child. **40**:1053 (Nov.) 1930.
9. Trendelenburg: Hormone, Berlin, Julius Springer, 1929, p. 193.

which seemed to show that the amount of injury to the suprarenal determines the changes in temperature. Comparatively slight injuries do not influence the temperature. Complete destruction of both glands may result in collapse and subnormal temperature, leading to rapid death. The failure of Arnold to observe the characteristic syndrome of suprarenal hemorrhage in the new-born infant might be explained on the basis of the physiologic experiments quoted.

The observations in this case on the chemical changes of the blood deserve attention. A low blood sugar can safely be interpreted as being due to impairment of the suprarenals, apparently to that of their medullary portion. Greenwald and Pennell [10] noted a drop in the blood sugar content to 44 mg. in 100 cc. of blood forty-eight hours before the onset of clinical signs in an infant that subsequently died of bilateral suprarenal hemorrhages. Four hours before death the blood sugar was as low as 10 mg. in 100 cc. of blood. This case will be reported in *Endocrinology* by Drs. M. A. Goldzieher and M. B. Gordon.[11] A low blood sugar is also one of the characteristic findings in chronic suprarenal insufficiency, that is, Addison's disease. Another peculiar feature was the high figure for nitrogen metabolites, which decreased as soon as improvement set in. According to Hartmann,[12] suprarenal insufficiency in animals is accompanied by nitrogen retention, which is relieved by the administration of cortical hormone. Hartmann even suggested the use of this as a test for the assaying of the cortical hormone.

Recovery of a new-born infant after suprarenal hemorrhage has frequently been observed. It stands to reason that such recovery can take place only if the suprarenal glands are not too severely damaged. Recovery is more common in unilateral hemorrhage, and it seems that the case reported here belongs to this group.

SUMMARY AND CONCLUSIONS

A case of suprarenal hemorrhage in the new-born infant is reported, presenting the characteristic syndrome of high temperature, rapid respiration and a palpable tumor mass in the abdomen. The infant recovered spontaneously.

A chemical study of the blood may aid in the diagnosis, a low blood sugar and nitrogen retention being significant of damage to the suprarenals.

575 Ocean Avenue.

10. Greenwald, H. M., and Pennell, S.: The Carbohydrate Metabolism of the Normal New-Born Infant, Am. J. Dis. Child. **39**:281 (Feb.) 1930.

11. Goldzieher, M. A., and Gordon, M. B., personal communication.

12. Hartman, F. A.: Endocrinology **14**:229 (July) 1930.

Progress in Pediatrics

BLOOD STUDIES IN INFANTS AND IN CHILDREN

I. ERYTHROBLASTIC ANEMIA; A CLINICAL AND PATHOLOGIC STUDY *

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Introduction
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INTRODUCTION

Erythroblastic anemia is a disturbance of the hematopoietic system characterized by a constant racial and familial incidence, a typical facial appearance, a progressing anemia with large numbers of nucleated erythrocytes in the peripheral blood, enlargement of the spleen, distinctive changes in the bones and, finally, histologic lesions in the bone marrow and spleen.

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* From the Infants' and Children's Hospital and the Departments of Pediatrics and Pathology of the Harvard Medical School.

The symptom complex is presumably not an entirely new one, but has been classified previously as atypical familial hemolytic anemia, as pernicious anemia, as splenic anemia and as von Jaksch's anemia or "pseudoleukemia infantum." The last name has been associated with many disturbances in infancy and childhood characterized by anemia, splenomegaly and the presence of immature cells in the peripheral blood. As this group of findings is not uncommon in a variety of diseases, the diagnosis has served for many etiologically unrelated conditions. In view of the use of the name "von Jaksch's anemia" in even the more recent literature to describe well recognized cases of erythroblastic anemia, it is a fair surmise that cases of erythroblastic anemia have been labeled thus previously and so lost for future reference. The cases reported originally by von Jaksch differ in many respects from erythroblastic anemia. In his cases, large numbers of circulating nucleated erythrocytes were not a prominent or constant feature. The ultimate prognosis was good, the patients usually making a complete recovery, whereas in erythroblastic anemia, the prognosis is poor and to date no patient has been known to recover. The patients seen by von Jaksch and his associates, contemporaries and followers were most probably not of Mediterranean ancestry. Certainly no mention is made of any such possibility. The characteristic facial and skeletal changes so striking in patients with erythroblastic anemia should not have escaped recognition, and yet no mention of this finding was made either in the original descriptions of von Jaksch's anemia or in any subsequent accounts. These are sufficient reasons for discarding the term pseudoleukemia infantum.

REVIEW OF THE LITERATURE

Cooley[1] and his co-workers called attention, in 1925, to erythroblastic anemia and pointed out that it constitutes a disease entity distinct from the large group of "splenic anemias" seen in infants and children. In a later communication, Cooley,[2] in discussing the question of von Jaksch's anemia, said that the condition in question, the salient clinical and pathologic features of which he described, seemed to be the only definite disease entity to be distinguished in the miscellaneous group of cases reported as "von Jaksch's disease," Though he did not believe it to be the disease von Jaksch attempted to describe, he suggested that it might be worth while to give von Jaksch's anemia a definite status

1. Cooley, T. B., and Lee, P.: Tr. Am. Pediat. Soc. **37**:29, 1925. Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

2. Cooley, T. B.: von Jaksch's Anemia, Am. J. Dis. Child. **33**:786 (May) 1927.

by limiting the term to this disease, rather than to coin a new name. Finally,[3] he pointed out that this term was not suited, and he suggested the name "erythroblastic anemia" because of the outstanding hematological change—nucleated erythrocytes in large numbers in the circulating blood. His reported cases 1, 2, 3, 5 and 6 are undoubted instances of erythroblastic anemia. Case 6 is from this clinic and is included in the present series, with details as to the subsequent course. Cases 4 and 7, both by racial descent and from a study of the subsequent course, were shown later not to be of this group.[4]

One of the first cases that may be recognized in the literature as erythroblastic anemia was described in 1917 by Stillman.[5] The diagnostic criteria mentioned were: an Italian child, with marked anemia, numerous nucleated erythrocytes in the blood, an enlarged spleen and liver, a normoblastic crisis after splenectomy that persisted and histologic changes in the spleen characteristic of this form of anemia. The subsequent course of the patient was compatible with the diagnosis, although the continued relative fair health and activity over so long a time are unusual and make this patient the oldest now living with a known case of this disease.[6] Mention is not made of the facial appearance, and the roentgenologic changes in the bones are not reported. The other two cases reported by Stillman in the same paper are doubtful instances of erythroblastic anemia. Not all of the necessary criteria for establishing the diagnosis are given, and the complete recovery of the third patient is against the possibility of its having had erythroblastic anemia.

Hitzrot,[7] in 1928, added three cases to those previously reported. They occurred in children of Italian parentage, members of the same family. Their clinical, hematological, roentgenologic and pathologic findings were all typical of the disease, as were the subsequent courses.

Whipple, Reeves and Cobb,[8] in 1928, added two case reports. Their patients were Italian girls, sisters, who presented all the findings present in erythroblastic anemia, including pathologic changes in the spleens.

Wollstein and Kreidel,[9] in 1930, reported, as von Jaksch's anemia, nine cases similar to those described by Cooley. Eight of their patients

3. Cooley, T. B.: Resemblances and Contrasts in the Hemolytic Anemias of Childhood, Am. J. Dis. Child. **36**:1257 (Dec.) 1928.

4. Personal communication to the authors.

5. Stillman, R. G.: Am. J. M. Sc. **153**:218 (Feb.) 1917.

6. Personal communication to the authors: The patient is now 25 years old, married and keeping house and is in relatively good health. The blood shows a moderate anemia and large numbers of nucleated erythrocytes.

7. Hitzrot, J. M.: Ann. Surg. **88**:361 (Sept.) 1928.

8. Whipple, A. O.; Reeves, R. J., and Cobb, C. C.: Ann. Surg. **88**:380 (Sept.) 1928.

9. Wollstein, M., and Kreidel, K. V.: Familial Hemolytic Anemia of Childhood—von Jaksch, Am. J. Dis. Child. **39**:115 (Jan.) 1930.

were of Italian, the other of Greek, parentage, and there was a familial history in five instances. The hematological findings in each case were consistent with erythroblastic anemia. The report of roentgen examination of the bones, however, was given in only three cases, two of which showed a rarefaction, and the other, no abnormality. Splenectomy was performed on five of the patients without apparent benefit. The changes in the blood picture following removal of the spleen were not given.

Whitcher,[10] in 1930, reported three cases as "erythroblastemia of infants." However, roentgenologic changes were not described, and although there were numerous nucleated erythrocytes in the peripheral blood of each patient when first examined, these cells were absent in two after blood transfusions. Also no mention of the nationality of the patients was made, and no description of their facial appearance was given. There is, therefore, some doubt as to whether or not these cases should be classified as erythroblastic anemia.

Parmelee [11] has reported two cases, both in Italian children, in which the findings of mongoloid facies, pale brownish skin, moderate anemia and roentgen changes in the long bones and skull suggest erythroblastic anemia. However, there appear to have been very few nucleated erythrocytes in the peripheral blood in one child, and their presence or absence in the other child is not mentioned.

Brief discussions of erythroblastic anemia based on the findings in the cases here reported have been given previously.[12]

Vogt and Diamond [13] have given a full description of the changes in the bones demonstrable by roentgen examination in erythroblastic anemia, comparing them with the similar, but less striking, changes seen in the bones in congenital hemolytic anemia and sickle cell anemia.

Mandeville [14] has described in detail the changes in the skeletal bones in erythroblastic anemia as shown by roentgenologic examination in four cases. The clinical findings are to be reported later.

Capper,[15] in 1931, reported two cases that bring out points of considerable interest. Case 1 occurred in an Italian boy in whom a severe form of malaria developed at the age of 9 months, which, however,

10. Whitcher, B. R.: Am. J. M. Sc. **179**:236 (Feb.) 1930.

11. Parmelee, A. H.: Anemia with Peculiar Bone Changes in the Skull, Tr. Chicago Pediat. Soc., 1930; Am. J. Dis. Child. **39**:1364 (June) 1930.

12. Blackfan, K. D.; Baty, J. M., and Diamond, L. K., in Oxford Monographs on Diagnosis and Treatment, New York, Oxford University Press, 1930, vol. 9, p. 531. Baty, J. M.: New England J. Med. **203**:319 (Aug. 14) 1930.

13. Vogt, E. C., and Diamond, L. K.: Am. J. Roentgenol. **23**:625 (June) 1930.

14. Mandeville, P.: Radiology **15**:72 (July) 1930.

15. Capper, A.: Am. J. M. Sc. **181**:620 (May) 1931.

was cleared up by treatment with quinine. When seen at 2½ years, he presented the findings typical of erythroblastic anemia. Following splenectomy, there was a marked erythroblastic crisis, which has persisted for six months. The usual histologic changes in the spleen are not described. The previous infection with the malarial parasite seems to have been coincidental rather than an etiologic factor in this case, as the child was born and lived in a country where malaria is not infrequent.

The second case, also in an Italian child, is of interest because at the age of 8 months there were splenomegaly, anemia and nucleated erythrocytes in the peripheral blood. At about 2 years, these findings were more prominent; however, typical changes in the facies and in the roentgenograms of the skeletal bones seemed to be absent. The blood findings, both before and after splenectomy, were consistent with those of erythroblastic anemia. The description of the histologic examination of the spleen does not mention erythrogenic activity. Further observation will aid in classifying this case accurately.

Many other examples of this disease undoubtedly have been reported as von Jaksch's or as splenic anemia, but as incomplete hematological, clinical or roentgenologic data are presented in most instances, it is difficult to pick them out of the literature. There are at present reports of twenty-six cases that may be classed as erythroblastic anemia. In five additional cases, the data are incomplete, and such as are given seem to rule out this disease. With the twenty cases that we now add, this makes a group of forty-six cases in all.

CLINICAL AND PATHOLOGIC ASPECTS

The following data were obtained chiefly from the sixteen cases studied in this clinic, from cases (four) seen by us in other Boston clinics [16] and from the cases reported previously.

Age.—The onset, as determined by the appearance of symptoms, may occur at any time during the first decade of life, most commonly during the first two years. In thirteen of sixteen cases, symptoms began before the age of 2 years, and in the remaining three, at 2½, 3 and 4 years, respectively. The average age at the onset of symptoms in the sixteen cases was 16 months. The average age at the time the patients were brought to the hospital, however, was 34 months.

Incidence.—There is no definite predominance in either sex. Thirteen of our group were females, and seven were males. No instance of hereditary transmission has been recorded. The familial and racial fac-

16. Two patients with this disease were seen at the Massachusetts General Hospital through the courtesy of Dr. Harold L. Higgins and two others at the Boston City Hospital through the kindness of Dr. George R. Minot.

tors, however, are extremely interesting. Two of these patients were twin sisters, apparently "identical," two were brothers, two were sisters, and three were brother, sister and first cousin. In two other instances, there was suggestive evidence of familial incidence, which could not be verified.

Twelve of the patients we have seen were of Greek parentage, six of Italian, one of Armenian and one of Sicilian. This racial limitation, that is, to people of Mediterranean countries, is one of the constant features of this disease. There are no reports of cases occurring in other races. The majority of the recorded instances has been of Greek parentage.

Symptoms.—The onset of symptoms in erythroblastic anemia is gradual, occurring during infancy or in early childhood. Because of language difficulties, the history obtained from the parents is often scanty, and the exact time of onset is apt to be indefinite unless it is noticed following an acute illness. In addition, certain factors interfere with the early recognition of a diseased state in these patients. These are, chiefly, the naturally dark complexion of people of Mediterranean origin, which may easily overshadow moderate degrees of pallor, and the frequent occurrence of prominence of the abdomen in children of these races, due either to rickets or to early malarial infections or other tropical diseases. The first abnormality in the child's condition that is noticed by the family is usually pallor. This is so slight in degree at the beginning that it excites no alarm in the majority of cases until other symptoms have developed. The pallor gradually becomes more marked and is often accompanied by slight yellowness of the skin. The yellowness does not increase to any extent and is not of sufficient degree to be termed "jaundice." Enlargement of the abdomen, usually progressive, is frequently noticed, and may be the presenting symptom. This enlargement results chiefly from the increase in size of the spleen and liver. Constipation of varying degree is often present and is a troublesome factor at times. The increasing pallor and enlargement of the abdomen may be accompanied by weakness and increased fatigability associated with general malaise. Unexplained attacks of feverishness occasionally occur, and loss of appetite and vomiting are more rarely prominent symptoms. Such complaints as precordial pain, abdominal pain, dyspnea on exertion and enlargement of the head are present in some instances. Pathologic fractures of the bones of the extremities are very rare, but do occur. In two instances (cases 18 and 19), there was roentgen evidence that such fractures had occurred in the past.

Physical Findings.—Patients with erythroblastic anemia may be well nourished. Physical development is retarded after the first year of life, the height-weight ratio being definitely less than normal. The mentality is normal as judged by the reaction of the patient to the environment.

The general appearance is so unusual and so strikingly similar that a presumptive diagnosis can often be made by inspection. The patients bear a greater resemblance to each other than to the normal members of their own families (figs. 1 to 6). There is a moderate degree of pallor of the skin and mucous membranes with a sallow, but not actually yellow, tint. Certain characteristics at once attract attention: (1) The facies is mongoloid: The eyes are prominent; there may or may not be an epicanthal fold; the malar eminences are high; the nose is short, with a depressed bridge; the complexion has a peculiar muddy pallor. (2) The head is large and irregularly shaped with prominent frontal and parietal bosses, and, in cases of long standing, there is a sulcus-like

Fig. 1 (case 1).—A Greek child of 4 years, with a characteristic facies, mongoloid in type. The eyes are prominent and the lids puffy. There is an epicanthal fold. The forehead is high, with prominent frontal bosses.

depression in the upper surface of the skull, along the superior sagittal suture line, caused by the widening of the diploe on either side. (3) The stature is small, and the general bodily development is retarded. (4) The abdomen is prominent.

There is generally a slight degree of enlargement of the peripheral lymph nodes. Small, discrete, nontender glands, from 1 to 3 cm. in diameter, are usually palpable in the cervical and inguinal regions, and may be present in the axillary and epitrochlear spaces.

At the time of hospitalization, the heart is practically always enlarged, the rate is increased, and hemic murmurs are present. As

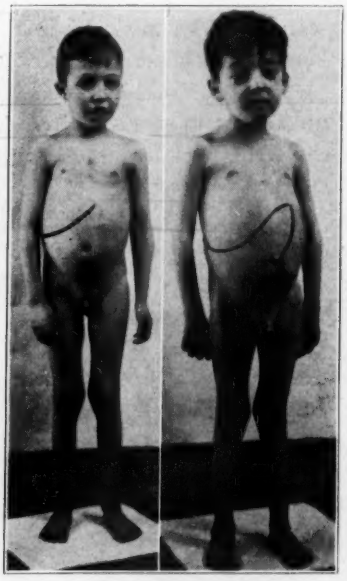

Fig. 2 (cases 2 and 3).—Brothers of Greek parentage, aged 8 and 7 years. The lines over the abdomen indicate the edge of the liver, and in the younger child, that of the spleen also. The facial appearance is more striking in the younger of the two children.

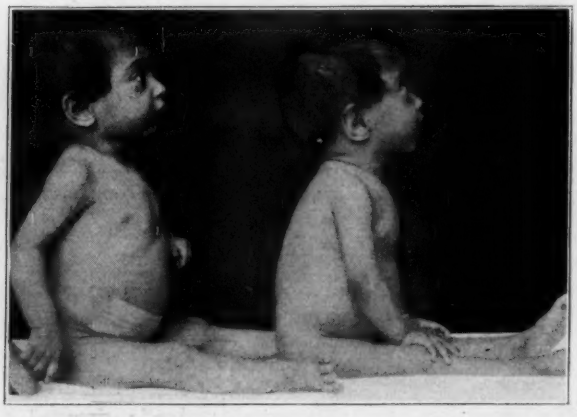

Fig. 3 (cases 4 and 5).—Infant twins of 11 months, of Greek parentage. They have the characteristic facies, with a high forehead and prominent frontal and parietal bosses, giving a "square-shaped" head.

Fig. 4 (cases 6 and 7).—Sister and brother, aged 6 and 2 years, of Italian parentage. They present a characteristic appearance. The older child is obviously poorly developed for her age. The lines over the abdomen indicate the size of the liver and spleen.

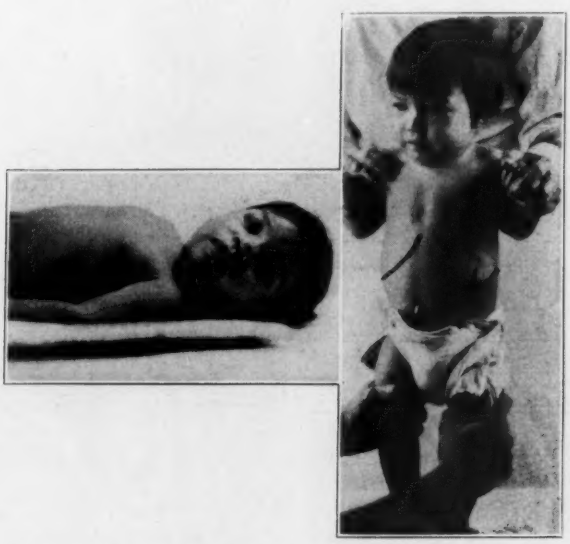

Fig. 5 (case 9).—An Italian infant. The photographs were taken at the ages of 8 months and 2 years, respectively.

these changes in cardiac signs are secondary to the anemia, they vary considerably in different patients and at different times in the same patient.

The abdomen is protuberant, more so on the left than on the right, owing to the large spleen. The veins may be abnormally prominent, and an umbilical hernia is often present, as the result of increased intra-abdominal pressure.

The spleen is greatly increased in size, is firm and smooth and has a sharp border. The splenic notch can usually be palpated. The size of the spleen varies, tending to increase gradually as the disease

Fig. 6 (case 10).—An infant, aged 3 years, of Sicilian parentage. Attention is called to the similarity in facial appearance of the children shown in these photographs in spite of the age and racial differences.

progresses. As a rule, it extends downward to about the level of the umbilicus, but may be enlarged only 1 or 2 cm. below the costal margin, or may extend below the pelvic brim and forward across the midline. The liver is also increased in size, but to a lesser degree. The border is rounded, rather soft and not tender.

Roentgen Findings.—Examination of the skeleton by the roentgen rays reveals certain changes that are constant and characteristic. They vary in degree in different patients and in different bones of the same patient, with a tendency to become more marked as the disease progresses.

The long bones show unusually prominent medullary trabeculations, especially at the metaphyseal ends of the diaphyses. This is most marked in the small bones, the metacarpals and metatarsals, because of the better detail obtained in roentgen-ray films (fig. 7). The changes can be recognized here most easily and in the earliest stages. The total width of the bone is definitely increased, owing to the widening of the medullary portion, which shows rarefaction and increased trabeculation (fig. 8). The cortical portion, however, is markedly thinned and occasionally presents punched out areas. When the process is more advanced and the cortex is exceedingly thin, pathologic fractures may occur.

Fig. 7.—Roentgenogram of the hand. The characteristic changes in the bones as shown by the x-rays are illustrated: widening of the medullary portion; increased radiability with prominent trabeculations; extreme thinning of the cortices.

The cranial vault, in the early stages of the disease or in the milder cases, shows only a slight thickening and an increased porosity of all the bones with thinning of the tables (fig. 9). In the advanced stages, the depth of the bony structure is greatly increased (figs. 10 and 11). The outer table becomes so thin and porous that it cannot be detected as a distinct plane. The diploe is very prominent and seems to extend beyond the outer table. The profile view of the skull then gives the appearance of a surface studded with small radiating spicules perpendicular to the tables of the skull. This fuzzy outline is described best

by the phrase, "hair standing on end." The rest of the skull plate has a fine spongy appearance.

There are irregular trabeculations, increased porosity and radiability in the bones of the pelvis, the vertebrae, the ribs, the clavicles and the scapulae.

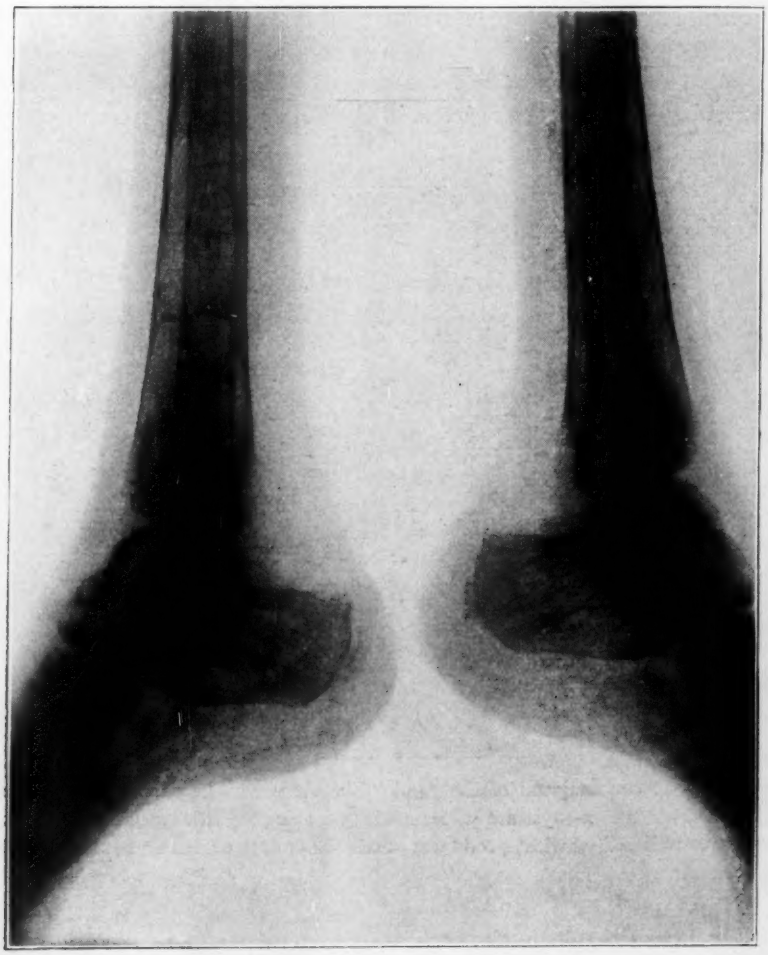

Fig. 8.—Roentgenogram of the lower legs. The changes are more advanced than those in figure 7. (From the collection of Dr. T. B. Cooley.)

Hematological Data.—The blood shows an anemia of varying degree directly proportional to the duration and the severity of the clinical symptoms. The erythrocyte count may be between 1,000,000 and 4,000,000 per cubic millimeter, being most commonly between 2,000,000 and 3,000,000. The hemoglobin percentage is relatively low, usually

from 25 to 45. The color index, therefore, is low. The blood platelets are normal or moderately increased in numbers, rarely being at a low normal level. They number, as a rule, from 200,000 to 400,000 per cubic millimeter by the more commonly used methods of counting. A leukocytosis is almost constantly present. The white blood cell count is usually between 10,000 and 25,000 per cubic millimeter, but may be as high as 50,000. Nucleated erythrocytes are always present in

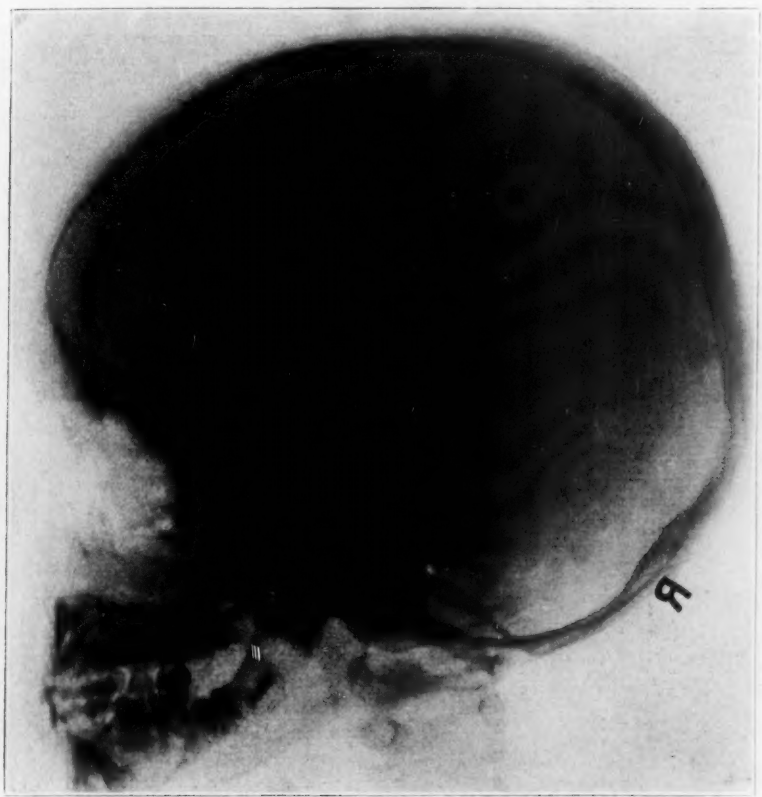

Fig. 9.—Roentgenogram of the skull. Note the thickening of the bones, the earliest recognizable change in the skull. (From the collection of Dr. T. B. Cooley.)

the peripheral blood, numbering from a few hundred to 125,000. As the leukocytes and nucleated erythrocytes cannot be differentiated in the blood-counting chamber, the total count is constantly high and must be corrected by a differential count of the cells in a fixed stained smear of the blood (figs. 12 to 15).

The differential leukocyte count shows a preponderance of cells of the myeloid series. These cells form from 60 to 90 per cent of the

white blood cells. The majority are polymorphonuclear leukocytes, many of which are young forms, so-called metamyelocytes. There are a few myelocytes and more rarely myeloblasts. Eosinophils and basophils are constantly present in small numbers and may be moderately increased above the normal. The percentage of lymphocytes is relatively decreased, being usually from 10 to 30. The majority are small, adult forms, although large, young lymphocytes may be present. The percentage of monocytes is also relatively low, being from 1 to 5.

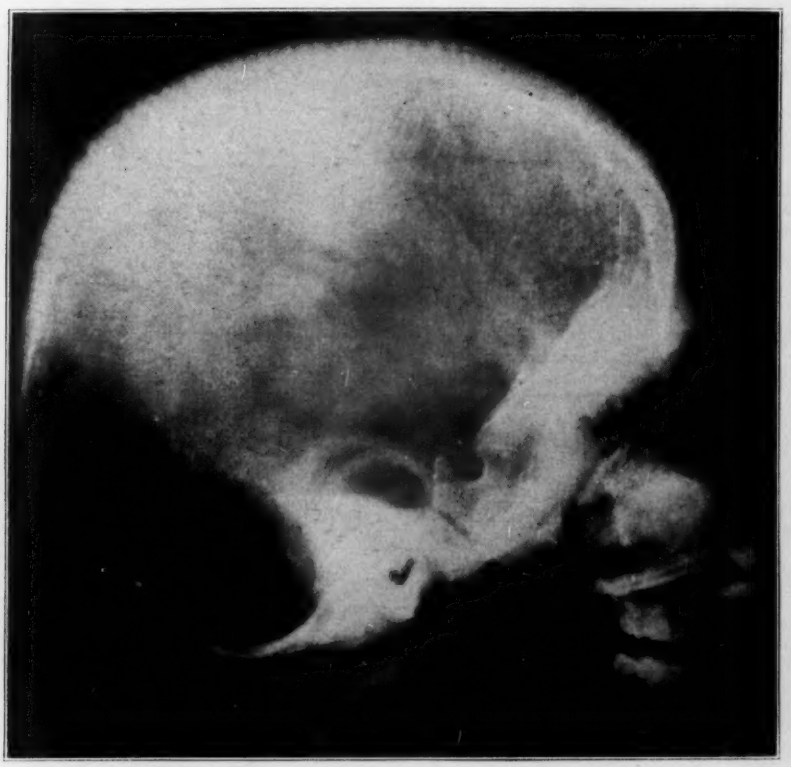

Fig. 10.—Roentgenogram of the skull. The changes are more marked than those in figure 9, with spicule formation and partial obliteration of the outer table. The decreased density of the bone is shown in the ramus of the mandible.

The changes in the erythrocytes, as seen in the stained film of blood, are most remarkable and present a memorable picture. There is a marked degree of achromia associated with an extreme variation in the size and shape of the cells. Macrocytes and microcytes are present in large numbers. As noted, there are numerous nucleated red blood cells: megaloblasts, erythroblasts and normoblasts. It is not unusual to find some of these cells containing two nuclei, suggesting amitotic division.

Mitotic figures are not present. There is an accompanying increase in other forms of immature erythrocytes. Polychromatophilic cells are numerous, and, when stained with brilliant cresyl blue, from 5 to 15 per cent of the erythrocytes show reticular material, an increase in the percentage as well as the total number of reticulocytes. The granule cells are increased, and cells containing Howell-Jolly bodies are frequently encountered. More rarely, cells containing Cabot's ring bodies are seen. A few cells show basophilic stippling. The blood platelets are present in normal numbers and often are increased in size.

Fig. 11.—Roentgenogram of the skull. The changes are in an advanced stage. The bones are widened, owing to an increase in the medullary portion. The inner table is clearly shown, from which innumerable radiating spicules extend outward. (From the collection of Dr. T. B. Cooley.)

The total number of white blood cells and nucleated erythrocytes, the percentage of immature forms and the degree of achromia, anisocytosis and poikilocytosis tend to increase, coincident with progression in the severity of the anemia and of the clinical manifestations of the disease.

Hematological Data Following Splenectomy.—Striking changes occur in the peripheral blood following removal of the spleen, which has been done as a therapeutic measure in several instances. The

erythrocyte counts and hemoglobin percentages remain essentially unaltered, although in some cases there seems to have been a slight but persistent increase. The total number of leukocytes and the percentage of immature forms increase rapidly for from ten days to two weeks after operation, and then decrease slowly to slightly above the preoperative level. The number of nucleated red blood cells, however,

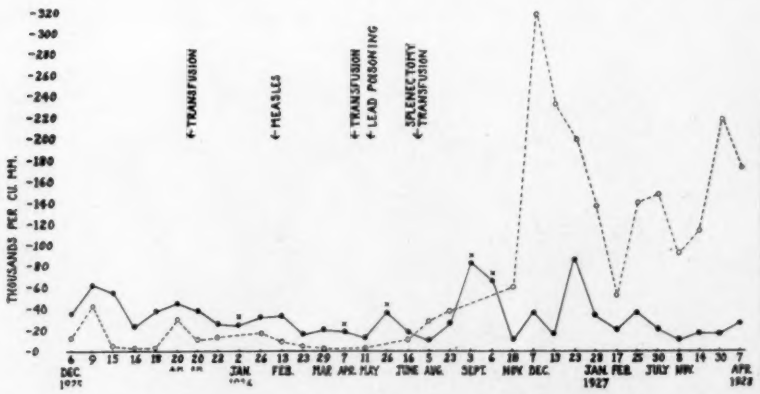

Fig. 12 (case 1).—The solid line represents leukocytes; the broken line, nucleated red blood cells; the asterisk, uncorrected, total nucleated cell counts. Note particularly the persistent leukocytosis, the large number of nucleated erythrocytes and the tremendous increase in the latter following splenectomy.

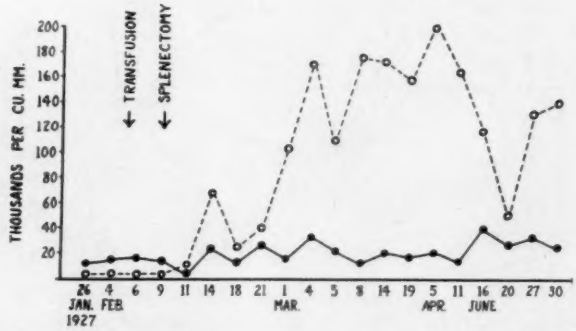

Fig. 13 (case 2).—The solid line indicates leukocytes; broken line, nucleated red blood cells.

rises sharply following splenectomy and remains above the previous level, these cells constituting from 50 to 90 per cent of the total nucleated cell count. The persistence of the nucleated erythrocytes in extraordinary numbers after removal of the spleen is graphically shown in figures 12 and 13. There is a coincident rise in the number of other immature erythrocytes and a marked increase in the anisocytosis and

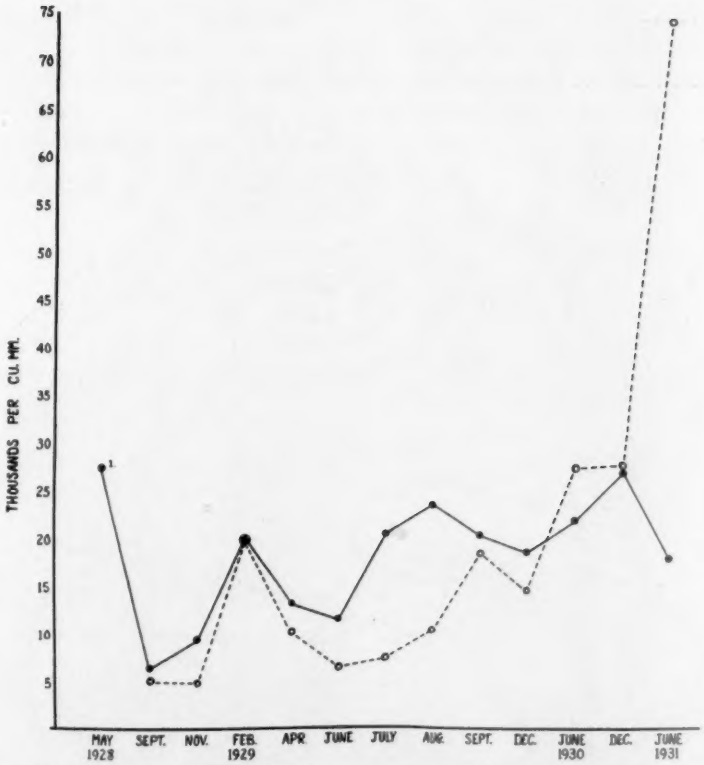

Fig. 14 (case 6).—The solid line represents leukocytes; the broken line, nucleated red blood cells. Count *1* is the uncorrected total nucleated cell count. Note the gradual increase in the number of nucleated erythrocytes over the three year period; these cells now form 80 per cent of the total nucleated cell count.

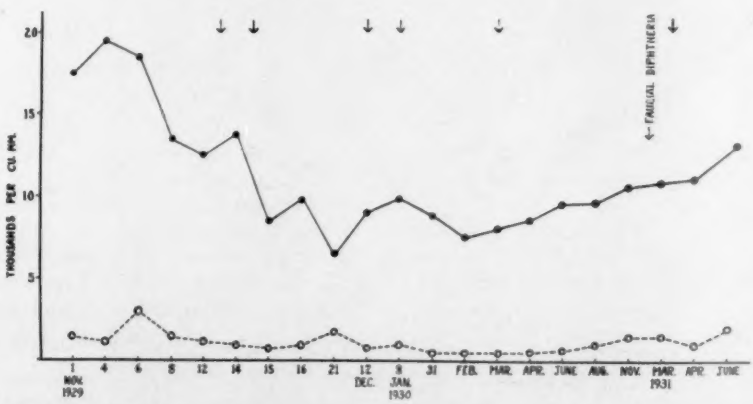

Fig. 15 (case 10).—The solid line indicates leukocytes; the broken line, nucleated red blood cells. The arrows indicate the time of roentgen treatments over the spleen. There has been no appreciable change in the total number of nucleated erythrocytes over a two year period.

poikilocytosis, so that often it is impossible to find a normal-appearing adult erythrocyte in the stained film of blood (fig. 16). The blood platelets increase in number and remain very little altered for an indefinite period after splenectomy, whereas the changes in the blood after removal of this organ in other types of anemia are very transitory.

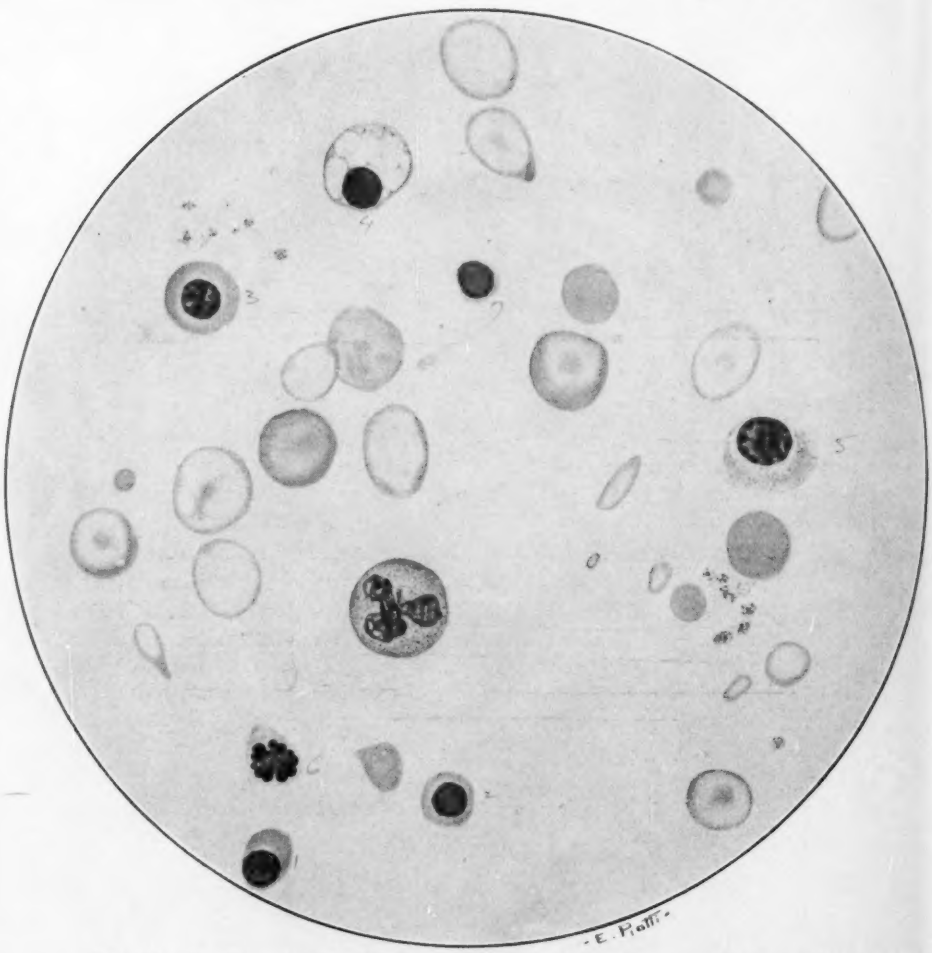

Fig. 16.—Drawing from a blood smear in case 1, taken one year after splenectomy. There is an extreme variation in size, shape and staining of the erythrocytes. Seven nucleated red blood cells are shown at different stages of development.

The icteric index of the blood is normal or only slightly increased. The bleeding time and the coagulation time are normal. In hypotonic saline solutions, the erythrocytes exhibit a definite prolongation of the "resistance span." The resistance span of the red blood cells of the normal person is from about 0.46 to 0.34; that is, hemolysis begins in

0.46 per cent sodium chloride solution and is complete in 0.34 per cent solution. The resistance span of the erythrocytes of the patients with erythroblastic anemia, on the other hand, is usually from 0.54 to 0.28, or even greater; that is, hemolysis begins in 0.50 to 0.54 per cent sodium chloride solution and is complete in 0.30 to 0.20 per cent solution, but may not be complete even in distilled water.

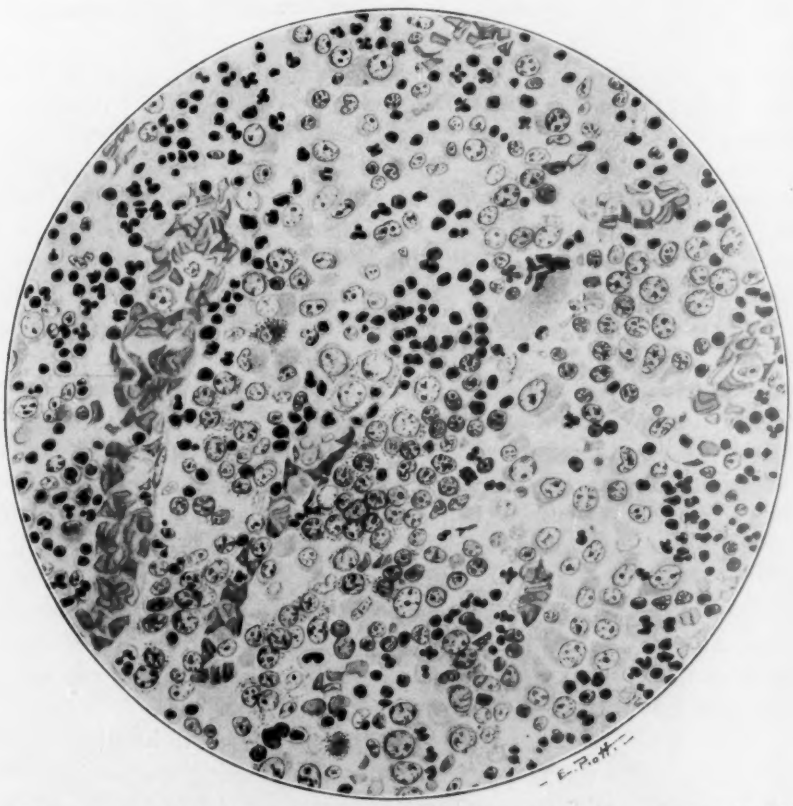

Fig. 17 (case 3).—Camera lucida drawing from the bone marrow; × 700. Erythropoietic hyperplasia, clusters of large, undifferentiated cells and large numbers of nucleated erythrocytes are seen.

Other Laboratory Data.—The urine and stools usually show an increased urobilinogen content at one time or another, indicating abnormal hemolysis. Analysis of the gastric contents may reveal hypochlorhydria, but not complete anacidity, a normal secretion of hydrochloric acid occurring after the subcutaneous injection of histamine. Other laboratory tests yield normal results. Although it is possible for a patient with erythroblastic anemia to have tuberculosis

or syphilis, in this series the tuberculin tests and Wassermann reactions have been negative. Malaria has been present in two of the reported cases.

Pathology.—The description of the pathologic changes is based on the study of the spleens removed at operation in six patients, the bone marrow obtained by biopsy in three cases and complete necropsy material from one patient. The essential changes other than those attendant on any long-standing anemia are confined to the bone marrow and other organs involved in hematopoiesis.

Bone and Bone Marrow: Macroscopically, the cortex of the long bones and sternum is found to be extremely thin. The red marrow tissue may be seen shining through a very thin translucent bone layer when the periosteum is removed. This finding is further emphasized by the ease with which the cortex of the bone may be incised with a sharp scalpel. The marrow cavity is greatly widened and filled with dense red marrow tissue. Trabeculae of bone project into the marrow cavity, particularly in the later stages of the disease. These produce the cross-striations seen in the roentgenograms. Microscopically, the marrow is extremely hyperplastic with a great predominance of the erythrocytic elements (fig. 17). Clusters of young undifferentiated cells, apparently the forerunners of the erythrocytes, are scattered throughout. Mitotic figures are numerous. These immature cells are surrounded by circles of easily recognizable nucleated red blood cells at varying stages of maturation. This confirms the identification of the undifferentiated cells as erythrogenic. The proportion of nucleated to nonnucleated red blood cells is greatly increased over that seen in normal marrow tissue. There is also active myeloid formation, and megakaryocytes are numerous. The complete absence of fat cells in normal bone marrow tissue is very striking. The general impression received is that of a rapid overgrowth of cells, mostly erythrogenic.

Sections of the bone marrow of these patients have been compared with those of the bone marrow from patients with pernicious anemia. The latter sections were from the collection of Dr. Francis W. Peabody, obtained by bone marrow puncture and at necropsy at different stages of the disease. As described by Dr. Peabody,[17] during the stage of remission in pernicious anemia, the bone marrow is relatively normal, while during relapse there is extreme hyperplasia of the erythrogenic substance. The microscopic picture of the marrow in erythroblastic anemia is practically identical to that in pernicious anemia during the stage of relapse, and it is impossible to differentiate the sections from the two conditions.

17. Peabody, F. W.: Am. J. Path. **3**:179 (May) 1927.

Spleen: The spleen is enlarged from three to seven times the normal. The weight varies from about 100 to 700 Gm. (The spleen of the normal child of 2 years weighs 30 Gm., and of the 12 year old child, 90 Gm.) It is firm and dark red. Thickening of the capsule and a fibrous perisplenitis are often present. The cut surface is firm and red, and the malpighian corpuscles are readily identified. Microscopic examination reveals an increase in fibrous tissue, varying in amount. The pulp is abundant and cellular, containing all types of leukocytes and erythrocytes. There is extensive hematopoiesis, chiefly erythrocytic, as evidenced by scattered, very young, undifferentiated cells occurring for the most part in islands surrounded by large numbers of nucleated erythrocytes at different stages of development (fig. 18). Numerous mitotic figures are present in these clusters of young cells. Small groups of similar young cells are seen within the sinuses. In many instances these cells seem to arise from the sinus endothelium. Polymorphonuclear neutrophils and neutrophilic myelocytes, as well as large numbers of eosinophils and eosinophilic myelocytes, are present. There are scattered lymphocytes and plasma cells. Megakaryocytes are occasionally seen. There is a varying amount of hemosiderin deposit, although this is usually small in amount. Large phagocytic cells sometimes may be seen. The sinuses are prominent and partly filled with leukocytes and erythrocytes. The splenic corpuscles are few, and for the most part are inactive, although active germinal centers may be encountered occasionally.

These features, that is, fibrosis, extensive erythropoiesis, an increase in the number of eosinophils, hemosiderin deposits and atrophy of the follicles, have been present so uniformly in the spleens of patients with this disease that together they constitute a distinctive pathologic picture.

The distinctiveness of the histologic changes was brought out by a comparison with the pathologic histology of sixteen spleens removed at operation from patients with congenital hemolytic anemia, anemia of the Banti type, splenomegaly with gastric hemorrhages and idiopathic purpura hemorrhagica. The chief difference was in the erythropoietic activity, which was practically negligible in the latter groups, and the more constant atrophy of the germinal centers and the greater number of eosinophils and eosinophilic myelocytes in the spleens of patients with erythroblastic anemia. Fibrosis and hemosiderin deposits occurred irregularly and to about an equal degree in the spleens of the various groups.

Liver and Lymph Glands: The liver likewise may show evidence of extramedullary hematopoiesis, especially in the advanced stages of the disease. The outstanding change, however, is extensive fatty degeneration of the liver cord cells. The lymph glands may take part in the extension of erythrogenic activity, but to a slighter degree.

Course and Prognosis.—Erythroblastic anemia is a chronic disease, although the duration and severity of symptoms vary widely in different cases. It begins in early infancy, often continuing throughout childhood

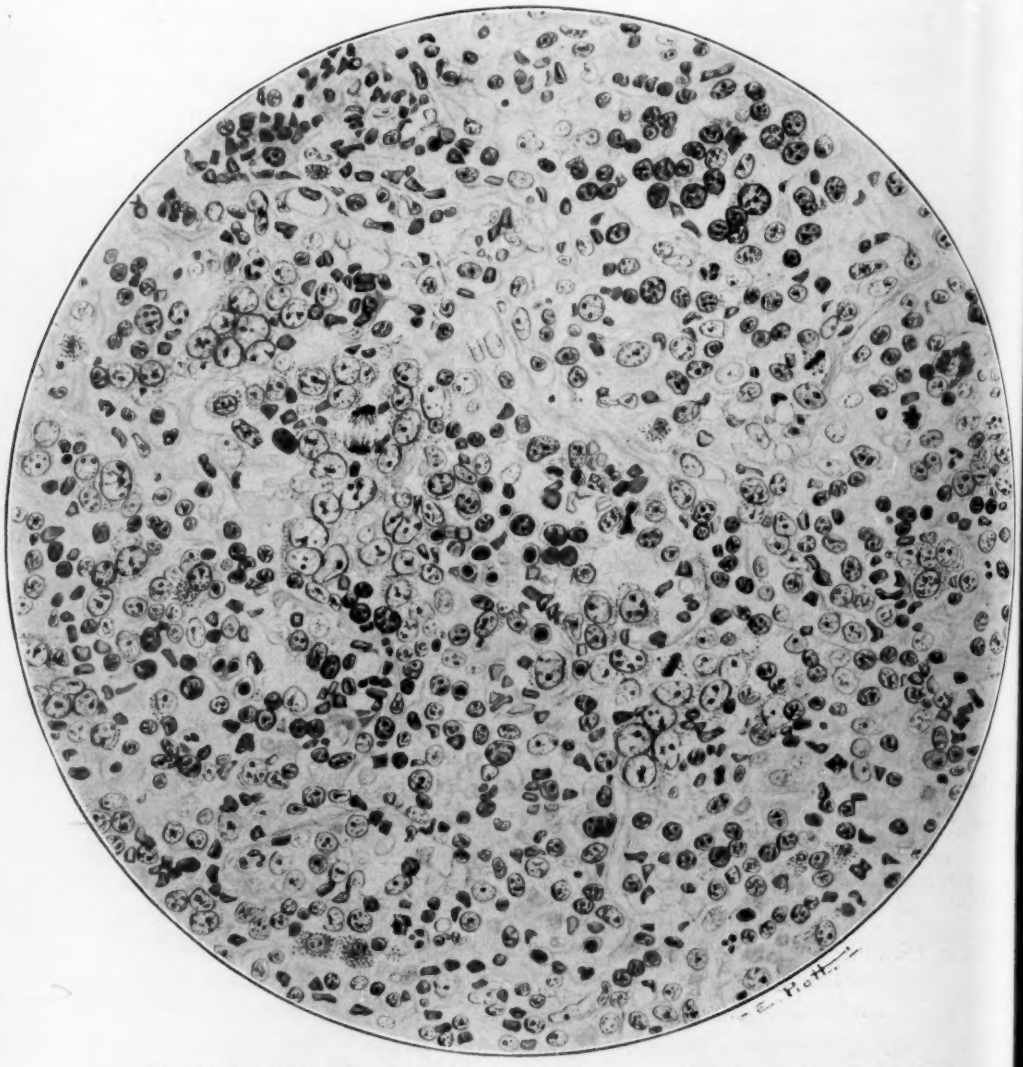

Fig. 18 (case 3).—Camera lucida drawing from a section of the spleen × 700. Islands of large undifferentiated cells (apparently megaloblasts), many mitotic figures, large numbers of nucleated red blood corpuscles and numerous eosinophils and eosinophilic myelocytes are seen.

and rarely into adult life. Relatively mild symptoms, most commonly pallor and enlargement of the abdomen, may be present for months or even years before medical advice is sought. In several instances the

condition has been recognized during the course of some unrelated disease for which the patient was being examined.

In general, it would appear that the course is more acute in the patients in whom the disease is recognized during the first year of life. The average total duration in four patients in whom the diagnosis was established under 1 year of age was sixteen months, as compared to forty-five months in eleven other cases (figured to January, 1931, as several of the latter group are alive). There is no definite tendency to remissions or exacerbations, although the symptoms are apt to become more severe coincident with intercurrent infections. The occurrence of such infections, however, does not seem more common among this group of patients than in other groups of the average population of comparable ages. A majority of the patients contracted acute infections of the upper respiratory tract from time to time; a few rather frequently. Two of the children weathered attacks of acute primary pneumonia, and one had a severe attack of measles followed by pneumonia, from which he made an uneventful recovery. Another was brought to the hospital primarily because of symptoms due to acute pyelitis. However, these patients show unusual periods of hyperpyrexia of varying duration for which no adequate explanation is discovered. During such times the temperature varies from 101 to 104 F., the patient appears acutely ill and is somewhat prostrated, and the anemia becomes more severe. These elevations in temperature are comparable to the so-called Pel-Epstein syndrome seen in Hodgkins' disease.

There is a gradual, almost imperceptible, progression of symptoms over a period of months or years, and the patient finally succumbs to an intercurrent infection or to acute dilatation of the heart, probably secondary to the long-standing anemia. Death may occur suddenly as a result of thromboses following removal of the spleen (cases 3 and 9).

Differential Diagnosis.—In the presence of the clinical findings as outlined, there should be no difficulty in the recognition of erythroblastic anemia. Conversely, the diagnosis should not be made in the absence of any of the essential characteristics, that is, anemia in children of Mediterranean races, accompanied by enlargement of the spleen, nucleated erythrocytes in the peripheral blood and changes in the bones demonstrable by roentgenologic examination.

It should be emphasized that the hematopoietic system is very labile and reacts readily to various stimuli throughout the period of infancy and to a less extent during childhood. Consequently, immature cells of all types may appear in the peripheral blood with greater ease than in adults, and the presence of these young cells is not necessarily an indication of disease primarily involving the blood-forming organs. One of the conditions most likely to produce confusion is anemia of

severe degree secondary to infection or dietary deficiency, or both, in an infant. In such cases, the hematological findings may resemble those seen in erythroblastic anemia. An Italian infant, 18 months of age, was seen in this clinic recently, in whom a severe anemia existed as a result of the combination of three factors: prematurity, dietary deficiency and repeated infections. The blood smears showed occasional nucleated erythrocytes, a moderate degree of achromia, anisocytosis and poikilocytosis and many immature leukocytes. However, there were no changes in the skeleton demonstrable by roentgenograms, and following adequate therapeutic procedures the course was quite unlike that of erythroblastic anemia. In this case, the absence of changes in the bones demonstrable by roentgen examination was an important aid in establishing an early diagnosis.

In congenital hemolytic anemia and in sickle cell anemia, changes in the bones somewhat similar to those in erythroblastic anemia, but much less marked, may be encountered. The other features common to each of these diseases are sufficient, as a rule, for differentiation. However, the atypical cases that do not present the classic findings may require observation over a longer period of time in order that a correct diagnosis be established. Congenital hemolytic anemia (familial hemolytic jaundice) may occur early in childhood. However, the absence of a distinct racial incidence, the presence of greater numbers of reticulocytes (usually above 15 per cent) with relatively few nucleated erythrocytes, the increased fragility of the erythrocytes in hypotonic saline solutions, the evidences of increased hemolysis, i. e., a high icteric index, visible jaundice and large amounts of urobilin in the urine and stools, and finally the striking and usually lasting benefit obtained from splenectomy should differentiate congenital hemolytic anemia from erythroblastic anemia. Sickle cell anemia occurs in people of the negroid race and may be diagnosed by the presence of the sickling phenomenon in the erythrocytes. These positive findings and the absence of the blood changes so characteristic of erythroblastic anemia should differentiate these conditions.

Leukemia has been suggested often by brief physical examination and study of the blood film of the patient with erythroblastic anemia. Leukemia may present, among other things, an anemia, a large spleen, a palpable liver, immature forms of erythrocytes as well as leukocytes in the peripheral blood and roentgen changes in the bones, though these are not quantitatively or qualitatively similar to those found in erythroblastic anemia. Also, in leukemia, there is no constant racial or familial incidence. The immaturity of the leukocytes is the striking feature, and the presence of erythroblasts is purely incidental to the irritative infiltration of leukemic cells in the bone marrow. In erythroblastic anemia, the changes that are outstanding are in the erythrocytes, that is, the

extreme anisocytosis and poikilocytosis and the presence of the numerous nucleated erythrocytes. The number of myelocytes and more immature leukocytes is relatively small. Another important differentiating point is that in leukemia as it occurs in childhood one of the earliest recognizable changes is the thrombocytopenia with the tendency to purpuric manifestations. In erythroblastic anemia, the platelets are not reduced in number, and there is no tendency to the development of purpura. Leukemia in infancy and in early childhood is usually an acute disease, whereas erythroblastic anemia lasts months or years.

Pernicious anemia rarely, if ever, occurs in infancy or early childhood, whereas erythroblastic anemia is most common in this age group. The occurrence only in Mediterranean peoples, the typical facies, the presence of free hydrochloric acid in the gastric contents, especially after the injection of histamine, the numbers of nucleated erythrocytes, the roentgenologic changes in the long bones and skull and, finally, the failure to respond to liver or potent liver extract in large doses are all features present in erythroblastic anemia and absent in pernicious anemia that should serve to differentiate these two diseases.

Treatment.—The treatment for erythroblastic anemia is entirely symptomatic. The patient should be given an adequate well balanced diet, and attention should be paid to general hygienic measures. As the course of the disease when untreated tends to be chronic and the severity of the symptoms varies widely in different patients, it is difficult to evaluate accurately the efficacy of the diverse therapeutic measures that have been attempted.

The addition to the diet of iron and liver in large amounts may produce slight improvement in the anemia and thereby better the general condition of the patient. This effect is not striking, however, and in many instances no definite benefit is derived from either iron or liver or both, even when given in large amounts over a long period of time. Iron may be administered in any one of several easily obtainable forms, such as iron and ammonium citrate, reduced iron, ferric chloride or pills of ferrous carbonate. The double salt, iron and ammonium citrate, has the advantage of dissolving easily. It may be added directly to the milk or administered in water or orange juice. Ill effects do not occur after its use except for a slight diarrhea in rare instances. From 30 to 60 grains (2 to 4 Gm.) of this preparation should be given daily for a period of about three weeks and then smaller amounts daily for an indefinite period. Liver may be given in from 50 to 100 Gm. amounts daily. Liver extract even in large doses has proved to be of no appreciable value in the treatment for this condition.

Removal of the spleen of patients with erythroblastic anemia has failed to alleviate the symptoms or to cause improvement to any extent

except in the cases reported by Hitzrot. The remarkable changes in the peripheral blood following splenectomy have been pointed out. In the cases with extraordinary enlargement of the spleen, removal may relieve symptoms produced by the mechanical effects of the enormously enlarged organ, such as pressure or traction on the other viscera.

Therapeutic exposures to the roentgen rays has not been used sufficiently to judge accurately of the effectiveness. However, in the few patients treated in this manner over a short period of time, there has been no appreciable benefit.

Transfusion of blood produces transient relief of the symptoms referable to the severe anemia, but results in no lasting benefits. It is particularly helpful in patients with acute dilatation of the heart as a result of the severe anemia with possibly a superimposed acute infection. The immediate symptoms are relieved temporarily, but may recur at any time.

COMMENT

The etiology of erythroblastic anemia is obscure. The racial, congenital and often familial incidence suggests that it is the result of some inherited developmental defect in the hematopoietic system, the nature of which is not understood. One interesting hypothesis is the following: During the height of the so-called Greek era of civilization, particularly during the reign of Alexander the Great, there was extensive colonization of all the Mediterranean countries by Greece. In view of this fact, the racial incidence of the disease suggests the possibility that erythroblastic anemia is an inherited disease limited to people of more or less direct Greek ancestry. The failure on the part of the patients to respond to any of the therapeutic procedures that have been tried lends further support to the theory of a hereditary defect.

The findings in the peripheral blood are indicative of an extremely hyperplastic bone marrow throwing out cells in a disorderly fashion. Microscopic examination reveals hyperplasia of the bone marrow, involving chiefly the erythroid elements. This overactivity of red blood cell formation in the bone marrow is added to by the assumption on the part of the spleen of erythrocytic hematopoiesis. To a slight degree the other functions of the bone marrow, that is, leukocyte and platelet formation, also are being carried on in the spleen.

The clinical, hematological and roentgenologic findings may be explained as secondary to the hyperactivity of the hematopoietic system that takes place largely in the bone marrow and spleen.

The peculiar yellowish pallor of the skin is probably due to the chronic state of moderately severe anemia combined with a constant subicteric color, affecting a patient whose natural racial characteristic is a dark skin. Next, the changes in the shape of the skull, consisting of

wide parietal bosses, depression along the median longitudinal sulcus and high malar eminences, are brought about by a thickening of the medullary portion of the bones of the skull, together with a compensatory increase in the width of the cortical bone. This likewise probably impinges on the orbital spaces, so that the eyes become prominent, and may be given a slightly slanted appearance, the suggestion of the mongoloid. The invariable presence of these distinctive facial and skeletal changes in the well advanced cases is the reason for the close resemblance of these patients to each other, a fact that often makes a presumptive diagnosis possible from the first view of the patient.

The occurrence of moderate cardiac enlargement (late in the disease) is dependent on the presence of a severe anemia over a long period.

The abnormally functioning bone marrow fails to deliver adult erythrocytes to the blood stream in response to the normal stimuli, but instead continually throws out young, atypical forms. Thus, although the activity of the bone marrow is increased, its functional efficiency is diminished. Anemia, therefore, ensues, accompanied by the presence of abnormal cells in the peripheral blood. The enlargement of the spleen is brought about by the increasing hematopoiesis within the splenic substance, probably an extension of the abnormal activity of the bone marrow.

The cancellous and cortical bone is relatively soft in the infant and young child and becomes eroded as the marrow expands. The changes in the bones demonstrable grossly and by roentgen examination are the result of the mechanical pressure of the hyperactive growing bone marrow. Thus, the medullary portion of the bones becomes broader than normal, while the cortical portion is thinned out, these changes becoming more marked as the disease progresses.

It is interesting to compare as far as possible the findings in erythroblastic anemia with those in other conditions that are somewhat similar.

Cooley considered erythroblastic anemia as hemolytic in nature and closely related to congenital hemolytic anemia. The evidences of hemolysis in the former condition, however, are relatively slight, and severe hemolytic crises do not occur. Whatever hemolysis does take place may be explained by the natural tendency of the organism to remove from the circulation and destroy all abnormal forms of erythrocytes. Since there are many such in this disease, hemolysis in excess of normal is of only secondary importance, just as is true in pernicious anemia. The anemia tends to be more constantly severe and the reticulocytosis not as great as in congenital hemolytic anemia. The behavior of the erythrocytes in hypotonic saline solutions differs widely in the two conditions. Changes in the bones, entirely similar to, but never so

severe as, those in erythroblastic anemia, do occur in the true hemolytic anemias in childhood. These changes in the bones, however, are secondary to the rapid expansion of hematopoietic tissue in the bone marrow and may be produced by any such condition beginning during the early years of life and lasting over a long period of time.

Erythroblastic anemia also has been compared with leukemia. In the latter disease, there is a marked, tumor-like overgrowth of one of the leukocytic elements of the hematopoietic system with cellular infiltration of the viscera similar to that in certain metastatic malignant conditions. An anemia and a sparsity of blood platelets develop from the encroachment of the tumor tissue on the erythrogenic and platelet-forming elements of the bone marrow. Immature and atypical leukocytes are thrown into the peripheral blood stream, usually in large numbers, and occasionally immature red blood cells appear. The hyperactivity of the hematopoietic system in erythroblastic anemia, however, is limited largely to the bone marrow and spleen. And, although erythropoiesis may occur in the liver and to a less degree in the lymph nodes, there is no involvement of the other viscera by an infiltrating process similar to that seen in leukemia. The two conditions are similar, however, to the extent that in each the fundamental change occurs in the blood-forming tissues: on the one hand, in the erythrocytic, on the other, in the leukocytic, element.

In certain respects erythroblastic anemia is analogous to pernicious anemia. The condition of the bone marrow in erythroblastic anemia is similar to that found in pernicious anemia during the period of relapse. Peabody's admirable description of the pathologic changes in the latter condition applies equally well to erythroblastic anemia. He pointed out that there is a "cellular hyperplasia of the bone marrow with a functional inefficiency." This "diminished functional activity" of the blood-forming tissues is reflected by an increasing anemia and the appearance of young and abnormal erythrocytes in the peripheral blood. The other changes characteristic of pernicious anemia are absent in erythroblastic anemia, and in the latter disease there is no improvement following the feeding of adequate amounts of liver or liver extract.

SUMMARY

A clinical and pathologic discussion of erythroblastic anemia, based on the cases reported in the literature and twenty additional cases, is presented.

Erythroblastic anemia is a disease entity of unknown etiology characterized by a racial, congenital and often familial incidence, enlargement of the spleen and to a lesser degree of the liver and peripheral lymph nodes, a slowly progressing anemia accompanied constantly by

large numbers of nucleated erythrocytes in the peripheral blood, peculiar changes in the bones, a characteristic facial appearance and, histologically, erythropoietic hyperplasia of the bone marrow and extensive erythropoiesis in the spleen.

REPORT OF CASES

In view of the number of cases, only the essential data are given so far as is possible, leaving out negative, unimportant laboratory reports. The changes in the bones as revealed by roentgenologic examination were entirely similar in the different cases except for degree. For the sake of brevity, therefore, and to avoid repetition, the detailed description of the roentgenograms is omitted, and only the degree of change is noted. The individual reports of the pathologic changes in the bone marrow and spleen and the description of stained films of blood are also omitted for the same reasons. A detailed description of these findings is presented under "Clinical and Pathologic Aspects." The details of family, birth and feeding histories are given only when pertinent.

The hemoglobin determinations on the blood were made, except when otherwise specified, by the Newcomer colorimetric method (100 per cent equals 16.92 Gm. of hemoglobin per hundred cubic centimeters of blood).

CASE 1.—L. Z., a boy, of Greek parentage, was brought to the clinic at the age of 33 months because of progressive pallor and swelling of the abdomen. One brother had died at the age of 1 year of an anemia similar to the patient's. The patient was regarded as a normal infant until, following pertussis at the age of 28 months, he failed to regain his normal activity and became pale and his abdomen became enlarged. As these symptoms became more noticeable, he developed difficulty in breathing on slight exertion.

Examination revealed an undernourished and underdeveloped child. The distinctive features were the short stature, extreme pallor, prominent abdomen and oriental facies. The facial appearance was due to prominence of the forehead and malar bones (fig. 1). There was a slight icteric tint to the sclerae. The superficial lymph glands were enlarged, but were discrete and not tender. The heart was enlarged, and there was a blowing systolic murmur. The liver extended 3 cm. below the costal margin. The spleen was firm, with a sharp, notched edge, and it extended 2.5 cm. below the level of the umbilicus.

Examination of the blood showed: hemoglobin, 30 per cent; erythrocytes, 2,072,000 per cubic millimeter; leukocytes, 34,300; nucleated red cells, 13,900. Roentgenograms of the bones showed changes of moderate degree, which increased steadily during the period of observation.

The patient was under observation for three years until he died at the age of 5½ years. Throughout this time, he exhibited periods in which the temperature was elevated, ranging from normal to 102 or 103 F., and attacks of dyspnea and extreme prostration occurred. At other times, he would be bright and active and had but slight evidences of the extreme anemia that persisted. Repeated tests for increased fragility of the red blood cells gave negative results. Various

therapeutic procedures were instituted: transfusion, massive doses of iron, liver extract, liver pulp and dietary measures were without effect as regards improvement in either the general condition or the hematological findings.

The spleen was removed six months after the first admission. The peripheral blood showed a most remarkable response (fig. 12). There was an outpouring of nucleated red blood cells and of blood platelets, which, instead of gradually returning to normal as is usual following splenectomy, persisted until death. Following the removal of the spleen, severe attacks of abdominal pain developed. In each attack the liver would become tender and much increased in size. Such attacks were believed to be due to partial thromboses of the portal veins. Necropsy was not obtained.

CASE 2.—H. K., a boy, of Greek parentage, was brought to the hospital at the age of 8½ years with the complaint of weakness and jaundice. A younger brother (case 3) was suffering from the same complaint. The patient was considered healthy until the age of 3 years, when he became "yellow." At the age of 6 years he became weak and had a sudden attack of precordial pain for which he was taken to the local hospital. There he was found to be anemic and was given a transfusion of blood. The jaundice and weakness persisted, and although he was allowed to return home, he was unable to attend school.

Physical examination revealed pallor with a slight icteric tint, mongoloid facies, a moderate generalized enlargement of the peripheral lymph nodes; enlargement of the heart, with an apical blowing systolic murmur, and a firm and nontender spleen, extending 8 cm., and the liver 4 cm., below the costal margin (fig. 2).

Blood counts showed: erythrocytes, 3,860,000 per cubic millimeter; hemoglobin, 45 per cent (Tallqvist); leukocytes, 12,200; nucleated red cells, 3,050; reticulocytes, 8 per cent. The urobilin in the urine and stools was found to be increased on several occasions. The icteric index was 15. Four fragility tests were done during a period of three months. Hemolysis began in 0.46 to 0.52 per cent sodium chloride solution and was complete in 0.25 per cent. In the control solutions, there was hemolysis in 0.49 to 0.37 per cent. Roentgenograms of the bones showed changes of moderate degree.

Two weeks after admission, the patient was given a transfusion of blood, and three days later the spleen was removed. There was a rapid rise in the number of nucleated erythrocytes in the peripheral blood, and these cells persisted, being present in large numbers in blood smears taken at home two years after splenectomy (fig. 13). Except for an unexplained elevation of temperature for five days, four months after the operation, there was no remarkable change in the patient's condition, and he was discharged five months after coming to the hospital. Two years later he moved to Greece.

CASE 3.—C. K., a boy, of Greek parentage, was brought to the hospital at the age of 7 years and 8 months, because of weakness and jaundice for three and a half years. An older brother (case 2) was admitted to the hospital at the same time with a similar complaint. The patient was considered well, until at the age of 4 years he was noticed to be yellow; he became weak and less active, and the abdomen gradually became enlarged. At the age of 5 years, he was in the local hospital for six weeks. During the following two years, there was no appreciable change in his general condition or appearance.

Physical examination revealed pallor, with a slight icteric tint; a mongoloid facies (fig. 2); a few small purpuric lesions over the forearms and the lower part of the right leg anteriorly; a moderate generalized enlargement of the peripheral lymph nodes; an enlargement of the heart, with a loud systolic murmur over the

entire precordium; the spleen, large and firm, extending almost to the iliac crest, and the liver 3 cm. below the costal margin.

Examination of the blood showed: red cells, 3,256,000 per cubic millimeter; hemoglobin, 45 per cent (Tallqvist); leukocytes, 13,450; nucleated erythrocytes, 1,550; reticulocytes, 4.2 per cent. The urine contained an increased amount of urobilin on several occasions, with a less marked increase after splenectomy. The icteric index was 26. Fragility tests of the red blood cells showed an increase in the resistance span, hemolysis beginning in 0.43 to 0.52 per cent sodium chloride solutions and complete in 0.20 to 0.32 per cent. Roentgenograms of the bones showed changes similar to but less marked than those of the brother.

During the first six weeks in the hospital, the patient had several irregular, unexplained elevations in temperature lasting a few days. Two months after entry, a transfusion of blood was given, and two days later the spleen was removed. There had been no remarkable change in the blood counts prior to operation. Afterward, however, the number of nucleated erythrocytes rose rapidly to 40,000 per cubic millimeter and remained at about this level. There was also a marked increase in the number of blood platelets, other counts being relatively unchanged.

About two months after splenectomy, the patient suddenly became acutely ill, complaining of abdominal pain and vomiting. Laparotomy was performed on the third day, and thrombosis of the mesenteric veins was found. He became rapidly worse and died a few days later.

Necropsy was performed twelve hours after death. There was complete thrombosis of the portal and superior mesenteric veins and their branches, with gangrene of that portion of the intestine giving rise to the superior mesenteric vein. The heart was moderately enlarged, but showed no other abnormality on gross or microscopic examination. Bone and bone marrow were obtained from the sternum, ribs, right humerus and right femur (see under "Pathology," p. 686). There were no abnormal findings of note in the other viscera.

CASE 4.—J. M., a girl, of Greek parentage, was brought to the hospital at the age of 11 months, because of "poor color" and swelling of the abdomen. She was one of four children, the elder two being well and apparently normal, but a twin sister having the same disease (case 5). A severe attack of pertussis had occurred at the age of 2½ months. At the age of 3 months, the patient's skin was noted to be yellowish. This had persisted and progressed. The urine had been dark occasionally. At the age of 5 months, the abdomen began to enlarge, and a hard mass was felt in the left upper portion which steadily increased in size.

Physical examination revealed a small child, with a pale yellowish skin, a square-shaped head with a depression along the median longitudinal suture, a mongoloid facies, a slightly enlarged heart with a systolic murmur at the apex and a large abdomen, with the spleen extending to the crest of the ileum and filling most of the left side (fig. 3).

Examination of the blood showed an erythrocyte count of 2,400,000 per cubic millimeter; hemoglobin, 24 per cent; leukocytes, 17,600, and nucleated red cells, 4,400. Roentgenograms of the skull and long bones showed early mottling and increased trabeculation.

Over the period of observation there was no improvement in the patient's condition with any type of therapy tried, except for a temporary benefit from intravenous blood transfusion. The anemia slowly progressed to a more severe state, the heart became more enlarged, the spleen increased in size, and the liver became palpable. Roentgenograms revealed a rapid increase in the changes in the skull and the long bones. Nucleated erythrocytes were constantly present in varying

numbers and tended to become more immature in type. The patient was taken home, where she died at the age of 18 months. From the observations of the family physician, death seemed to be the result of acute cardiac dilatation.

CASE 5.—M. M., a twin sister of J. M., entered the hospital at the same time with an identical history. The patient was restless and dyspneic. The skin was dusky and sallow, with a slight cyanotic tint to the mucous membranes. The head and facies showed the same type of abnormalities as the twin sister's (fig. 3). The heart was markedly enlarged to the left, the rate being very rapid, and a systolic murmur was heard all over the precordium. There were moist râles at the bases of both lungs. The abdomen was protuberant. The spleen extended to the pelvis and across the midline at the umbilicus. The liver was palpable about 5 cm. below the costal margin.

There were 2,600,000 red blood cells per cubic millimeter, 28 per cent hemoglobin, 29,000 white cells and 11,000 nucleated erythrocytes. The fragility test demonstrated an increased span of resistance of the red blood cells in hypotonic saline solutions. The icteric index was 5. Reticulocytes numbered 5 per cent. Roentgenograms revealed a marked enlargement of the cardiac shadow and moderately advanced changes in the skull and long bones.

The patient was given several transfusions in the first month, showing temporary improvement both in the anemia and in the cardiac condition. The course thereafter was steadily downhill. The anemia became more severe. Nucleated erythrocytes were present continually in about the same numbers as on admission. Roentgenograms showed an increase in the skeletal changes. The patient died at home at the age of 18 months, within a few days of her twin sister, with symptoms likewise suggesting cardiac failure.

CASE 6.—R. L., a girl, of Italian parentage, was brought to the outpatient department at the age of 3 years and 4 months because of pallor and enlargement of the abdomen. The patient was seen on the hematological service five months later and at regular intervals afterward. The family history was irrelevant. However, about one year later a first cousin, maternal, was treated in the hospital for the same condition (case 8), and about a year later it was found that the brother of the patient was also anemic (case 7). The patient had been considered healthy, except for questionable pallor, until gradual enlargement of the abdomen was noticed at the age of 2 years. Following an acute infection a year later, she failed to regain strength and lost weight, the pallor became pronounced, and a yellowish tint was noticed.

On examination, the child was found to be rather poorly developed and nourished. There was pallor of moderate degree with a yellow tint. The facies was mongoloid, with marked epicanthal folds and prominent cheek bones, and frontal and parietal bosses (fig. 4). There was a slight generalized enlargement of the peripheral lymph nodes. The heart was not increased in size; a blowing systolic murmur was present at the apex. The abdomen was protuberant; the liver was palpable 3 cm., and the spleen, which was firm and smooth, 17 cm., below the costal margin.

Examination of the blood showed: red cells, 3,900,000 per cubic millimeter; hemoglobin, 38 per cent; platelets, 250,000; leukocytes, 6,400; nucleated erythrocytes, 5,300; reticulocytes, 11.6 per cent. The icteric index was 10. There was an increase in the resistance span of the red blood cells in hypotonic saline solutions, hemolysis occurring in 0.54 to 0.32 per cent sodium chloride. Roentgenograms showed moderately advanced changes in the bones.

The patient was given iron and ammonium citrate, 3 Gm. daily, for several periods of one month each, and liver and liver extract for several other periods.

No effect on the general condition or on the blood was demonstrable. The anemia became somewhat more marked, with greater anisocytosis and poikilocytosis and more numerous nucleated erythrocytes (fig. 14). There was a slight increase in the changes in the bones as shown by roentgen examinations.

CASE 7.—L. L., a 16 months old Italian boy, the brother of one of our earlier cases (case 6), was thought to be well, and the changes in the blood were discovered while each member of the family was being examined. The birth and the feeding histories were not abnormal. There had been no previous illnesses.

At about the age of 11 months, the mother thought that the patient was slightly pale, but there had been no fatigue, jaundice, lack of appetite or any other symptoms for which the sister had been brought to the hospital.

On examination, the patient appeared fairly well developed and nourished and not ill. The skin and mucous membranes were definitely pale, but there was no icterus. The frontal bosses were prominent. There was a definite epicanthal fold to the eyelids, giving the face a mongoloid appearance (fig. 4). There were no palpable glands. The heart was of normal size; a systolic murmur was present at the apex. The abdomen seemed somewhat prominent. The spleen extended 1.5 cm. below the costal margin, and was firm and smooth. The liver was just palpable at the costal margin.

Examination of the blood revealed 4,500,000 erythrocytes per cubic millimeter, 47 per cent hemoglobin, 13,800 leukocytes and 1,400 nucleated red cells. Roentgenograms of the bones showed early, slight changes.

When the patient was last seen at the age of 2½ years, the parents had noticed enlargement of the abdomen in addition to the pallor. Otherwise, he was considered well. The spleen and liver had increased in size, and there were more numerous nucleated erythrocytes in the peripheral blood and a greater variation in the size and shape of the red blood cells in stained smears.

CASE 8.—P. C., a girl, of Italian parentage, was first seen at the age of 10 months because of pallor and yellowish color of about eight months' duration. The patient was a first cousin (maternal) of R. L. and L. L. (cases 6 and 7). The patient had been born at term by cesarean delivery. The development had been normal. Liver extract had been given for a month before entry.

At the age of 2 months, the patient had a "cold" with vomiting and diarrhea lasting from three to four weeks. At this time she was noticed to be slightly pale and yellowish. The color had varied. There had been unexplained periods of fever lasting five or six days during the two months previous to admission.

Physical examination revealed a chronically ill child, very pale with a slightly icteric appearance, but with no jaundice of the sclerae. The head seemed enlarged. The facies was of the mongoloid type. The heart was enlarged, and a blowing systolic murmur was present over the entire precordium. The abdomen was prominent, the spleen extending to the left iliac crest, and the liver almost reaching the right iliac crest.

Examination of the blood showed 2,700,000 red cells per cubic millimeter, 36 per cent hemoglobin, 15,000 white cells and 2,000 nucleated erythrocytes. The urine and stools contained an increased amount of urobilin at one examination. The fragility test of the red blood cells showed a slight increase in the resistance span. The icteric index was 8. Roentgenograms showed moderate changes in the skeletal bones.

The patient's condition did not change appreciably during a period of observation of two weeks. There was an irregular, unexplained elevation in temperature for five days. Liver extract in large doses was added to the diet for two weeks

without an appreciable effect on the reticulocytes, the nucleated erythrocytes or the total number of red blood cells. The patient was discharged; she gradually failed, and died four months later in a neighboring hospital. Necropsy was not obtained.

CASE 9.—C. N., a girl of Italian parentage, was brought to the hospital at the age of 7 months because of gradually increasing pallor of two months' duration. There had been no fever or jaundice, or abnormally colored urine or stools.

Physical examination revealed a well developed and nourished infant. The skin was pale and dark but not icteric. The head was of normal shape. The eyes had a suggestive mongoloid cast. The heart was normal except for a soft systolic murmur at the apex. The abdomen was protuberant. The spleen, which was firm, smooth and not tender, extended 7 cm. below the costal margin. The liver was just palpable at the costal margin (fig. 5).

Examination of the blood showed 2,300,000 red cells per cubic millimeter, 40 per cent hemoglobin, 10,000 white cells and 2,000 nucleated erythrocytes. A fragility test of the red blood cells showed an increase in the resistance span. Roentgen examination showed early changes in the bones and enlargement of the heart.

The patient had four or five short periods of unexplained hyperpyrexia. She benefited temporarily from four intravenous transfusions. There was a satisfactory gain in weight on a high caloric diet. She was then discharged from the hospital.

During the following year, there was very little change in the blood; the spleen and liver increased steadily in size. Roentgenograms showed an increase in the degree of involvement of the skull and long bones.

At the age of 2 years, the patient's spleen was removed chiefly because of its mechanical effects. The convalescence was satisfactory, and the patient improved in health for a time thereafter. There were a rapid rise in the number of nucleated erythrocytes and blood platelets and a temporary increase in the number of leukocytes following splenectomy. The patient was then discharged, and she died at home very suddenly about three months later.

CASE 10.—S. T., a boy, was brought to the hospital at the age of $2\frac{11}{12}$ years, because of repeated "colds" and a yellowish color for about two and a half years. The parents, the grandparents and the great grandparents had been born in Sicily. At the age of 3 months, the patient was acutely ill with "pneumonia" for about two weeks, after which he never seemed as well as previously. Slight pallor with a yellowish tint was noticed at the age of 7 months, and enlargement of the abdomen at 1 year. During the year before entry, he had gradually become irritable and fussy and had had several attacks of cough lasting a few days accompanied by feverishness. His appetite had been poor, and he had been constipated.

Physical examination revealed a rather poorly developed and nourished child. There was pallor of moderate degree with a muddy yellowish color. The facies was mongoloid, with slight exophthalmos and epicanthal folds and prominent frontal and parietal bosses (fig. 6). The heart was slightly enlarged; no murmurs were heard. The abdomen was protuberant, the liver being palpable 2 cm., and the spleen 3 cm., below the costal margin. The spleen was firm, smooth and freely movable.

Examination of the blood showed: red cells, 3,490,000 per cubic millimeter; hemoglobin, 49 per cent; platelets, 490,000; leukocytes, 17,300; nucleated erythrocytes, 1,400, and reticulocytes, 6.2 per cent. A fragility test showed an increase in the resistance span. The icteric index was 10. Roentgenograms showed changes in the bones of a moderate degree.

The patient remained in the hospital for two and a half weeks, and has been seen in the outpatient department frequently since. He has been given iron in

large doses and six therapeutic roentgen exposures over the spleen without apparent benefit. His condition has remained about the same, and there has been little change in the blood counts. Nucleated erythrocytes have been present in the peripheral blood constantly (fig. 15).

CASE 11.—V. S., a girl, of Greek parentage, was brought to the hospital at the age of 26 months because of gradually increasing pallor for one year. The skin had become yellowish, and the patient had failed to gain in weight or strength. Her appetite had diminished, and vomiting had occurred intermittently. Feverishness had been noticed for one week.

At the time of admission, the patient was acutely ill with moderately severe pyelitis, which subsided within a few days. There was marked pallor of the skin and sclerae with a muddy yellowish tint. The facies was mongoloid, with slight epicanthal folds and prominent frontal and parietal bosses, the latter producing a central depression along the superior sagittal sinus posteriorly. There was no enlargement of the peripheral lymph nodes. The heart was moderately enlarged and a systolic murmur was audible over the entire precordium. The liver extended 2 cm., and the spleen 3 cm., below the costal margin, the latter being firm, smooth and not tender.

There were 2,360,000 red blood cells per cubic millimeter and 28 per cent hemoglobin. There were 23,500 white blood cells and 700 nucleated erythrocytes. The percentage of reticulocytes was 7. The icteric index was 10. The resistance span of the red blood cells was lengthened. Roentgenograms showed moderately advanced changes in the bones.

The patient remained in the hospital for four weeks, and has been followed since in the outpatient department. As the acute infection subsided, there was some improvement in the general condition, with remarkably little change subsequently. There has been no recurrence of the pyelitis. She has been given iron and ammonium citrate, 3 Gm. daily, over a period of three weeks, on two occasions without appreciable benefit. The anemia has persisted relatively unchanged, and the number of nucleated erythrocytes in the peripheral blood has remained approximately the same.

CASE 12.—L. A., a girl, of Italian parentage, was brought to the hospital at the age of 20 months. At about 12 days of age the skin and eyes had become yellow and the stools light. The yellowness had not changed for sixteen months but had become less marked during the three months before entry. She had vomited frequently. Three weeks previously she had had a "cold" lasting about one week.

Physical examination showed a well developed, poorly nourished child with a high degree of pallor, with a muddy yellowish tint, mongoloid facies, a slight puffiness about the eyes, a moderate generalized enlargement of the peripheral lymph glands, a slight nasopharyngitis and tonsillitis, a heart enlarged, with a systolic murmur at the apex, the spleen, which was firm, extending to the level of the umbilicus and the liver 5 cm. below the costal margin.

Examination of the blood showed: red cells, 1,752,000 per cubic millimeter; hemoglobin, 30 per cent; leukocytes, 16,800; nucleated erythrocytes, 700; blood platelets, diminished in numbers in stained films; reticulocytes, 9 per cent. A fragility test of the red blood cells showed an increased resistance span. Roentgenograms of the bones showed changes of moderate degree.

While the patient was in the hospital, there was very little change in her general condition or in the blood cell counts. She was given daily exposures of ultraviolet light over a period of two months, iron in small doses (from 3 to 6 grains [0.145 to 0.4 Gm.] daily) by mouth and subcutaneous injection and four transfu-

sions of blood of from 90 to 300 cc. each. The spleen was removed five months after entry. Following operation, there was a rise in the number of nucleated erythrocytes in the peripheral blood. The patient's condition remained essentially unchanged, and she was discharged four months after operation. She was readmitted to the hospital a year later. There had been no notable change, and nothing new was discovered by physical or laboratory examination. The total count of nucleated cells in the blood was 45,800 per cubic millimeter. Many nucleated erythrocytes were noted, but the smears were not available for differential counts.

Three years later, the patient was visited by a member of the Social Service Department, who reported that she was thought to be well; she attended school regularly, ate and slept well and played actively. One month afterward it was learned that the patient had died rather suddenly at home at the age of 6 5/12 years. No further details could be obtained.

CASE 13.—A. K., a girl, of Grecian parentage, was brought to the hospital at the age of 18 months because of pallor and enlargement of the abdomen. One brother had died at the age of 5 years after an illness of two years' duration said to be "heart disease" and "blood disease." The patient had seemed well and had developed normally until the age of 1 year, when the abdomen was noted to be slightly larger than previously. During the subsequent five months, the enlargement gradually increased, and the patient occasionally cried as if in pain. One month before entry pallor was noticed.

Physical examination showed a well developed and nourished, not acutely ill child. There were a moderate degree of pallor, with yellowish-gray skin; a mongoloid facies, and pea-sized lymph glands palpable in the cervical, axillary and inguinal regions. The heart was enlarged to the left anterior axillary line. The abdomen was protuberant; the liver and spleen were firm and not tender, extending to the level of the umbilicus.

Examination of the blood showed: red cells, 2,730,000 per cubic millimeter; hemoglobin, 37 per cent (Sahli); white cells, 43,200; nucleated erythrocytes, 57,200. Reticulocyte counts and fragility tests were not done. Roentgenograms of the bones revealed changes of moderate degree.

The patient was given liver daily (120 Gm.) and one therapeutic exposure to the roentgen rays over the chest and one over the splenic area. There was no remarkable change in the erythrocyte count or in the hemoglobin percentage. The white blood cells numbered between 17,000 and 42,000, and the nucleated red blood cells between 4,000 and 40,000 per cubic millimeter. There were occasional unexplained rises in temperature to 101 or 103 F., at times sustained over periods of from two to three days. The patient was discharged after three months; the condition remained essentially unchanged, and she did not return to the clinic. It was learned later that she died at home at the age of 28 months.

CASE 14.—M. K., a 4 year old boy, of Greek parentage, was brought to the hospital on account of cough, fever and a swollen abdomen. At 8 months of age, he was noticed to be pale. At 1 year of age, he was in a hospital, where he was found to be anemic, and to possess a slightly enlarged spleen and evidence of rickets. At 18 months, there were marked pallor and a very large spleen. An examination of the blood showed many immature cells, which were thought to be suggestive of leukemia. During the following two and a half years, the pallor had slowly increased, the skin had become dark, and the head had increased in size, although bodily growth had been markedly retarded. The abdomen had become protuberant. Five days before entry, the patient had become irritable, weak and feverish, and cough, rapid respiration and finally orthopnea had developed.

Physical examination revealed a very poorly nourished and markedly underdeveloped boy, acutely ill, with orthopnea, restlessness and a severe cough. The skin had a muddy yellow color. The head was large, with prominent bosses and a depressed median ridge. The facies was distinctly mongoloid. The lips and mucous membranes were pale and slightly cyanotic. The heart was greatly enlarged. There were a gallop rhythm and a loud systolic murmur over the entire precordium. There were numerous coarse râles over the bases of both lungs. The abdomen was distended; the liver was very large and tender, and the spleen reached into the pelvis, practically filling the left side of the abdomen.

Examination of the blood showed 1,800,000 red cells per cubic millimeter, 24 per cent hemoglobin, 32,000 leukocytes and 111,000 nucleated erythrocytes. Roentgenograms showed advanced changes in the bones and marked cardiac enlargement.

The patient failed to improve and was taken home. He died within two weeks of his original entry, of cardiac failure and terminal pneumonia.

CASE 15.—R. de P., an Italian girl of 2 7/12 years, was brought to the hospital on account of a "funny-shaped head and large stomach." The previous illnesses were: measles at 1 year, pertussis at 15 months and mumps at 25 months.

After the attack of pertussis, it was first noticed that the child's head was irregular in shape and the abdomen was prominent. The head had become gradually more peculiar in shape and the abdomen more enlarged, the latter being occasionally tender to touch on the left side. No other abnormality was noticed.

Physical examination revealed a moderately well developed and nourished girl, with a muddy yellow complexion. The head was large and had very wide frontal and parietal bosses, with "cross-bun" shaped depressions over the vault. The facies was mongoloid. The heart was enlarged. The abdomen was prominent; the spleen was palpable at the level of the umbilicus, and the liver extended 3 cm. below the costal margin.

Examination of the blood showed: erythrocytes, 3,400,000 per cubic millimeter; hemoglobin, 43 per cent; white cells, 19,000, and nucleated red cells, 2,200. There were increased amounts of urobilin in the urine and stools. The fragility tests of the red blood cells showed an increased resistance span. Roentgenograms revealed marked changes in the bones and cardiac enlargement.

The patient was placed on a diet rich in liver and red meats, with the addition of reduced iron daily. During the following two and a half months, there was no gain in weight, and no appreciable change in the clinical findings or in the blood picture. She was then lost from observation.

CASE 16.—M. T., a girl, of Armenian parentage, was admitted to the hospital at the age of 3 11/12 years because of a mass in the abdomen, felt at 2 years of age, which was said to be the spleen by the family physician. The mass gradually enlarged during the following year, and the child became noticeably pale. She also became weak and tired easily. There were periods of feverishness, which were increasing in frequency.

Physical examination revealed a chronically ill child, with a pale yellowish-tinted skin. The head was square-shaped, with prominent frontal and parietal bosses and a longitudinal depression between them. The facies was mongoloid. The sclerae were not icteric. The heart was not enlarged; there was a systolic murmur at the apex. There was a generalized, moderate glandular enlargement. The abdomen was protuberant. A firm, smooth spleen filled the left side of the abdomen and reached to the iliac crest. The liver was palpable 3 cm. below the costal margin.

Examination of the blood showed: 3,000,000 red cells per cubic millimeter, 40 per cent hemoglobin, 10,000 white cells and 25,000 nucleated erythrocytes. The excretion of urobilinogen was slightly increased. Fragility tests of the erythrocytes showed repeatedly an increased resistance span. Roentgenograms revealed moderately advanced changes in the bones.

During the eighteen days of hospitalization, there was relatively little change in the clinical condition of the patient. She was given eight vials of liver extract (Lilly) daily for ten days with no appreciable effect. Shortly thereafter, the patient was taken home against advice. Information as to the subsequent course could not be obtained.

CASE 17.—K. K., a girl, of Greek parentage, was seen at the age of 2 years at the Massachusetts General Hospital. At 3 months of age, pallor with slight yellowness and weakness had been noted. At 1 year, the spleen had been found enlarged by the local physician.

Physical examination showed a poorly developed and nourished child with a yellowish pallor. The heart was enlarged, and there was a systolic murmur at the apex. The abdomen was protuberant. The liver was 5 cm., and the spleen 10 cm., below the costal margin, the latter being firm and smooth.

Examination of the blood showed: red cells, 1,650,000 per cubic millimeter; hemoglobin, 25 per cent (Sahli); leukocytes, 42,700; nucleated erythrocytes, 5,300, and reticulocytes, 7 per cent. Roentgenograms showed marked changes in the bones.

The spleen was removed. Subsequently, the patient gained weight, and her appetite improved. The anemia persisted, and there was an increase in the number of immature erythrocytes in the peripheral blood. She was admitted three years later because of a fracture of the femur following slight trauma. At this time blood counts showed 16,000 leukocytes and 32,000 nucleated erythrocytes.

CASES 18 and 19.—A. T. and P. T., sisters, of Greek parentage, aged 17 and 12 years, were seen at the Boston City Hospital. These children had been pale since infancy, and for several years had been known to have an enlargement of the spleen and liver. The younger child had had several fractures of the bones following only slight trauma during the preceding four years.

The blood of each showed severe anemia with many nucleated erythrocytes. Roentgenograms of the bones revealed changes of extreme degree; there was evidence in the bones of the extremities of healed fractures, more numerous in the younger child. Bone marrow was obtained from the sternum of each by biopsy for microscopic study.

The unusual features in these cases were the ages and the occurrence of pathologic features.

CASE 20.—T. C., a boy, of Italian parentage, was seen at the Massachusetts General Hospital at the age of 4 years. The clinical, hematological and roentgenologic findings were similar to those in the foregoing cases. The case history is not available.

ERYTHROBLASTIC ANEMIA

ADDITIONAL COMMENTS *

THOMAS B. COOLEY, M.D.
AND
PEARL LEE, M.D.
DETROIT

Further observation and experience with erythroblastic anemia have strengthened our conviction that it is a definite clinical entity, and, to judge from our own experience and reports, verbal and published, from other clinics, not rare in children of Mediterranean ancestry, especially the Greeks. We are glad to have our position fortified by the careful studies of Bāty, Blackfan and Diamond. Their paper is so complete and so thoroughly in accord with our present ideas that there seems to be no occasion for us to go over the whole ground in presenting at this time a few corrections of our original presentation and some additional observations.

NUMBER OF CASES AND RACIAL INCIDENCE

Our first report [1] comprised seven cases, five of which were from our clinic, one from Abt's and one from Blackfan's. All of the patients were of the Mediterranean races except the patients in cases 4 and 7 from our clinic. These two were the least characteristic of the group, and as we have had opportunity to reexamine them recently, we have come definitely to the conclusion that the original diagnosis was incorrect. On more thorough study, case 7 seems to be clearly a case of hemolytic icterus. We are not able to classify case 4. The patient had congenital syphilis; she received energetic treatment, under which the Wassermann reaction became negative, but the hepatosplenic picture was unchanged. After six years' observation the disease does not seem to be progressing. She is a stunted child, with moderate anemia, constant, rather marked jaundice, a high icteric index, large amounts of urobilin but no bile in the urine, slightly diminished fragility and only moderate enlargement of the liver and spleen. Examination of the blood shows constant,

* Submitted for publication, Sept. 16, 1931.

1. Baty, J. M.; Blackfan, K. D., and Diamond, L. K.: Blood Studies in Infants and in Children, this issue, p. 667.

1a. Cooley, T. B.; Witwer, E. R., and Lee, Pearl: Anemia in Children with Splenomegaly and Peculiar Bone Changes, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

moderate leukocytosis, considerable numbers of nucleated red cells and marked anisocytosis without excess of microcytes, but none of the large, pale, irregularly stained erythrocytes that we have come to look on as characteristic of erythroblastic anemia. There is no appearance of the increasing demineralization of hyperplasia of the bone and bone marrow. Like the subjects of hemolytic icterus, she is "more jaundiced than ill," and we are now inclined to view the condition as either an atypical hemolytic icterus or an unusual result of the syphilitic taint. Splenectomy has been advised and refused.

Of the remaining five of this first group we have found that one patient (case 5) whom we had supposed to be Italian was Greek, and we have information that Abt's patient, whose name we took to be Syrian, was probably Greek. Since the publication of our first report we have had six other clear cases, in which there was only one Greek patient, the rest being Italian or Sicilian. The small proportion of Greeks is probably due to the fact that we have many more Italians than Greeks in our clientèle. As a large part of the Italian population of Detroit comes from Sicily, we have thought it might be that Sicilians rather than Italians from the mainland are the subjects of the disease, and that this might be the reason for finding few cases that might belong in this group reported in the Italian literature. We have lost track of the families of three of our "Italian" patients. Of those in our own series whose derivation we know, we have had two Greeks, two Sicilians and two Italians.

The omission of our cases 4 and 7 leaves all the patients in the reported cases in the Mediterranean race group; this is, as Baty and his co-workers pointed out, a cogent argument against this condition being von Jaksch's disease. We are not inclined, however, to lay great stress on the limitation of this or any similar disease to a particular race. We have found [2] that sickle cell anemia, formerly supposed to be peculiar to Negroes, occurs in Greeks, and it seems to us likely that any disease in which there is a hereditary element, as there presumably is in this disease, is limited more by locality and association than by race. The first case is probably a "sport," and the spread from it naturally occurs first in the same locality and among people of the same race. If a similar "sport" occurs in another locality and another race, a second focus may arise. This theory assumes that in this disease, as in sickle cell anemia, there are persons with a latent tendency—a diathesis—as the disease itself is too fatal to allow its subjects to become parents.

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2. Cooley, T. B., and Lee, Pearl: Sickle Cell Anemia in a Greek Family, Am. J. Dis. Child. **38**:103 (July) 1929.

DISEASE PICTURE

The Blood Picture.—Red Cells: The red cell picture in this anemia is particularly striking. The predominating type of cell is very large with a markedly uneven distribution of hemoglobin. It resembles very much the cell which Piney [3] described and called the macronormocyte. He characterized it as a morphologic giant which is not functional on account of the defective supply of hemoglobin. Results obtained with a stroma stain developed in the laboratory here indicate that this cell has also an abnormal stroma. Perhaps this is the reason for the defective hemoglobin content. Frequently it has a nucleus either of the dense blue-staining type or having a radiate arrangement of the nuclear chromatin. Piney then calls it a macronormoblast. Some microcytes are found also. The only anemia of childhood presenting a similar picture is sickle cell anemia. In this disease the cell is not usually so large, but it shows the same uneven distribution of hemoglobin. It also gives the same results with the stroma stain.

Normoblasts in large numbers and a moderate number of megaloblasts are observed almost invariably. The exception occurs in cases of apparent extreme exhaustion of erythropoietic tissue with a very low red count in the terminal stages.

Reticulocytes are usually present in a considerable proportion, from 10 to as high as 30 per cent, but do not reach the figures sometimes obtained in hemolytic icterus and sickle cell anemia.

White Cells: Leukocytosis is almost constant and at times of high degree. The type of cell varies and is not characteristic. Our observations do not agree with those of Baty and his co-workers as to the predominance of the granular forms. In our experience the most striking thing is the frequent change from granulocytosis to lymphocytosis in the same patient at short intervals. At times two of our patients have had an aplastic picture with leukopenia and scarcity of polymorphonuclears and platelets.

Icterus Index.—Our patients seem to have shown, on the whole, a higher degree of serum pigmentation than those of the Boston series, the index being from 8 to 30 or even higher, though periods occur when it falls to normal. We have not found that the degree of pigmentation shows any relation to the number of normoblasts as it should if the theory we formerly advanced,[4] that these cells are peculiarly susceptible to hemolysis, were correct.

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3. Piney, A.: Recent Advances in Hematology, ed. 2, Philadelphia, P. Blakiston's Son & Company, 1928, p. 33.

4. Cooley, T. B.: Likenesses and Contrasts in the Hemolytic Anemias of Childhood, Am. J. Dis. Child. **36**:1257 (Dec.) 1928.

Fragility.—With one exception, in which the findings were normal, all of our cases have shown increased resistance. We have seen no case such as that noted by Baty and his co-workers of "prolonged resistance span" in which hemolysis begins earlier than normal, though we have seen hemolysis incomplete even with distilled water.

Pathologic Findings.—We have nothing to add to our former report and that of the Boston group.

Results of Splenectomy.—We have come to believe that splenectomy, in addition to relieving the child of the burden of the enormous spleen, may retard the progress of the disease. This operation was performed on four patients. One, an infant, died a week later of a streptococcus infection of the throat. Another, in case 5 of our first series, died of septicemia five years after the operation, having lived rather comfortably during most of the intervening time. The two still living, nearly two years after operation, seem to be in a period in which the disease is almost stationary, and certainly not advancing so fast as before operation. None of the five patients on whom operation was not performed are now living.

The Nature of the Disease.—While hemolysis is a constant and important feature, we are no longer inclined to consider the disease primarily a hemolytic disorder in the sense that hemolytic icterus is. The apparent relationship is greater to pernicious anemia and sickle cell anemia, and it seems to us probable that the urge to put forth quantities of immature cells and the resultant hyperplasia of erythropoietic tissue may be the result of some metabolic disturbance which compels these tissues to make "bricks without straw."

Pediatric Biographies

SAINTE-MARTHE

1536-1623

JOHN RUHRÄH, M.D.
BALTIMORE

Gaucher I, physician in ordinary to François I, had a son born at Loudon, in 1536, to whom he gave the name of Gaucher II, but who was often called Scevola Sainte-Marthe, or Sammarthanus. Sainte-Marthe was educated at the University of Paris and studied law at the University of Poictiers, after which he was employed most of the time by the government. He was treasurer of France at Poictiers in 1579 and deputy in the États de Blois, in 1588. He died at Loudon in 1623, and a statue of him was erected there in appreciation of his services. His funeral oration was delivered by Théophraste Renaudot, physician to the King and the founder of the first French newspaper, *Gazette de France*. Sainte-Marthe's twin sons became well known historians. He knew Scaliger and Ronsard and dedicated verses to them. A prolific writer, chiefly in Latin, of both prose and verse, he turned out quantities of elegies, epigrams, sylves and metamorphoses, which were published in Paris in 1569 and 1579. His verse has finish and excellence and one of his early works "Sylvarum" contains a rhymed rendition of the Hippocratic oath.

Sainte-Marthe was not a physician, but one of his sons in early infancy suffered from some serious malady and even the efforts of the most clever physicians were of no avail. The good brother then studied everything concerning infancy, and the results of his studies were embodied in his principal work "La Paedotrophia," printed in 1584 and dedicated to Henry III, King of France and Poland. At the instance of the King, he started a version in French, but it was never finished.

It was a popular work. Nicolas Andry, in his "Orthopaedia" (1742), stated that up to that time there had been twenty editions. There are two translations into English; one appeared anonymously in 1710, together with Quillet's "Callipaedia," and the other by Henry William Tytler, translator of "Callimachus," is dated 1747.

PÆDOTROPHIA;

OR,

THE ART OF

NURSING and REARING CHILDREN.

A POEM, IN THREE BOOKS.

Tranſlated from the Latin of

SCEVOLE DE ST. MARTHE.

With Medical and Hiſtorical Notes; with the Life of the Author, from the French of MICHEL and NICERON; his Epitaph; his Dedication of this Poem to HENRY III. of France; and the Epigram written on the viſit he had the Honour to receive from CHARLES I. of England, when PRINCE OF WALES.

BY H. W. TYTLER, M.D.

Tranſlator of CALLIMACHUS, and Fellow of the Society for the Encouragement of Arts, Manufactures, and Commerce.

Vos SANMARTHANI *divina poemata crebrâ*
Pertractate manu, doctoſque evolvite chartas;
Hic tuus Heliconis aquas, hic flumina Pindi
Tota bauſit; nullam non nervit Apollinis artem.

QUILLET

LONDON:

Printed, for the AUTHOR, by JOHN NICHOLS, Red-Lion-paſſage: And ſold by J. DEBRETT, Piccadilly; J. MURRAY and S. HIGHLEY, Fleet-ſtreet; T. N. LONGMAN, Pater-noſter-row; BELL and BRADFUTE, Edinburgh; and by all the principal Bookſellers in Great-Britain.

M.DCC.XCVII.

Title page of the English translation of "Paedotrophia."

The invocation in the 1710 edition is as follows:

> Tho' Sacred Nymphs, you're free from fond Desires,
> And feel no Flame but pure Immortal Fires;
> Tho' Virgin Pleasures are your sole Employ,
> And never can you know the Marriage Joy;
> Nor, when the smiling Infant's born, can prove
> A Parent's pious Care, a Mother's Love;
> Ye *Nine,* who haunt the sweet *Aonian* Spring,
> You I invoke, nor dare, without you, Sing.
> A Theam proportion'd to my Strength I chuse,
> A Child's the Subject of my humble Muse.
> While from the Cradle, I, in my lowly Lays,
> Teach how to feed the Babe, and how to raise,
> 'Till its loose Joints are knit, its Art'ries strong,
> And the grown Youth forbids my forward Song.
> Thou by whose Genial Heat all Nature lives,
> And Grace and Vigour from the Beams receives,
> Thy Vital Warmth into my Verse infuse,
> My Labours crown, and animate the Muse.
> Thee *Phoebus,* Father of the tuneful Throng,
> Accept my willing Vow, and own my Song.

This may be compared with Tytler's version:

> Ye sacred Nine! that on th' Aeonial hill
> With virgin cares alone your bosoms fill,
> Tho' your bright lives in purer aether led
> Forbid the pleasures of the nuptial bed,
> Tho' free from fond desires you ne'er shall prove
> A Parent's care, a Mother's tender love
> Nor know the pains of Childbirth nor the joy
> To rear the lisping girl or prattling boy,
> Yet, Nymphs immortal, leave such cares awhile,
> Inspire my song and on my labour smile,
> For, left by you, what heights can I explore?
> How touch the string, or trembling think to soar?
> Oh, lend your tuneful breath, with gentlest art
> Raise my slow voice and guide my willing heart
> While from an humble theme I seek the bays,
> A child the subject of my lowly lays;
> Teach me to sing how Infants should be fed
> How nurs'd, how cloth'd, and from the cradle bred.

The Tytler translation is about 100 pages long and is divided into books. The first book considers prenatal care of the child and mother, and birth. The second goes into the care of the infant, the usual advice on nursing, the nurse, the feeding of the child and directions for weaning. The third takes up the diseases in some detail: ranula, which must have been more common then than now; tonsillitis, which is ascribed to the nurse's milk; fever treated by giving lemonade, or oil of violets;

earache, treated by dropping warm violet oil into the ear, and milk and barley poultices used externally. Teething is treated with hare's brain, that sovereign remedy of the time, honey or the use of a coral ring.

Colic receives due attention along with worms. A few lines may be quoted:

> And if with racking Gripes his Belly's rent,
> The Gnawings in his Bowels to prevent,
> Warm Water, and the Parts aggriev'd foment;
> Or else anoint with Oil of Camomile
> His Belly, or with Oil of fragrant Dill,
> Or what old Olives o'er the Fire distil.
> For the kind Heat insinuates by degrees,
> And passed to th' afflicted Place with Ease;
> It drives the Cold out of the Porous Skin,
> and Dissipates the Winds that rage within.
> The Causes and Effects of this Disease
> It cures, and gives the patient Infant Ease.

It takes a real poet to make verses on prolapse of the rectum; try it if you do not believe it. Sainte-Marthe does it as follows:

> Why shou'd I name how the Posterior Pipe
> Is apt the Bounds in weakly Babes to slip?
> The Muscles, moistn'd when the Belly's loose,
> Their nat'ral Duty to discharge, refuse;
> And out the *Anus* hangs, a grievous Pain;
> Nor is it easily got in again.
> The Body bind, foment it when 'tis out,
> And gently with thy Hand replace the Gut.

The advice in infant care and diet is pragmatic and amusingly phrased. Witness the suggestions:

> When the Child's Diet shou'd be chang'd,
> What most resembles Milk, in Tast and Use.
> No good from any thing that's New expect,
> Unless you know that Newness to Correct.
> As Physick out of Poison may be had,
> So good may be the Mean, th' Extream bad.
> Broth may be oft and innocently us'd,
> And the soft Bread that's in the Broth infus'd.
> But Pap, the Infant's Dish, I most approve;
> This Nurses most commend, and Children love.
> With Milk and Bread the sooty Tin they fill,
> Stir it together o'er the Fire, and boil.
> They try it with a touch, the Spoon they dip,
> Blow it, and put it to his craving Lip.
> Sometimes the Bread they with a gentle Thumb
> Break, and in Broth or else with Butter crumb.

As he in Age and Strength or Body grows,
That Strength in time the use of Flesh allows.
Feed him, when minc'd, to ease the toothless Gum,
Some Meals on Flesh, and at the Nipple some;
His Hunger willingly with both supply,
But ben't deceiv'd, and do not trust his Cry;
For he's not always hungry when he Squalls,
And oft for neither Meat nor Drink he calls.
As when a Pin, which often happens, pricks,
Or Gripes his little Entrails tear, he shrieks.
Be not to fond of feeding him, but spare
The Spoon, nor love to lay your Bosom bare.
Don't you, as Mothers love, with frequent Food,
Above its strength, your Infant's Stomach load.
Thence puking Pains and other Ills arise,
While the crude Burthen undigested lyes.
And thus what Nature meant for Life's Support,
Cuts off his Days, instead of lengthning, short.
Observe due distances between his Meals,
Nor feed him when you find his Belly swells.
If you see Blotches rising on his Skin,
They shew the Load tha't undischrg'd within.
Perhaps e'en now he'll roar; why, let him roar,
And don't you feed him 'till he wants it more,
'Till Nature has consum'd the present Store.
Let him his Lungs, for Crying's useful, strein,
'Twill purge a heavy or a watry Brain.
Wash him a Nights, e'er you the Cradle make,
He'll sleep the sounder, and the sooner wake.
Stir him, and toss him, for an Infant's Sloth
Produces Rickets, and prevents his Growth.
If to be carry'd, he, by crying, begs,
Keep him, when he can go, upon his Legs.
And Prattle to him sometimes, sometimes sing,
Or to his Ear the tingling Coral ring.
Nor less to Dandle him and Dance forebear,
Nor keep him in the House, but give him Air.
When Western Winds with balmy Wings perfume
The Fields, and Heav'n invites, who'd stay at Home?
Shew him the painted Skies, their rolling Fires,
Tell him who made what he so much admires:
Teach him betimes to know his mighty Pow'r,
Betimes their Maker and his own Adore.

And certainly no pediatrician of the present day will object to these lines:

Call the Physician to your Aid; advise
With him, and do not think your self too wise;
Do not to ev'ry idle Tale attend,
Nor on old Womens Recipe's depend.
Too much the learn'd into this Error give,
Are thus deceiv'd themselves, and thus deceive.

Pediatrics in Art

CONGENITAL DEFORMITY

JOHN RUHRÄH, M.D.
BALTIMORE

Madonna and Child

Cranach (or Kranach) Lucas, the elder (1472-1553), was closely associated with his son, and it is not always possible to say which one painted the pictures ascribed to them. The painting reproduced here, photographed from the original in the Pinakothek in Munich, shows the Madonna and child, and curiously enough the foot of the latter reveals a marked deformity on the widely separated large toe and the one that adjoins it. This is one of the few congenital deformities figured in art. (The photograph is by F. Bruckmann, Munich.)

News and Comment

GENERAL

Camp for Handicapped Children in Michigan.—The W. K. Kellogg Foundation Camp for physically handicapped children will open at Pine Lake about July 1. Two hundred handicapped children can be cared for, for a two months' camping period. Dr. M. R. Kinde, medical director of the Barry County health unit, will act as director.

UNIVERSITY NEWS

Dr. Olimpio Cozzolino has been named professor of diseases of children at Parma.

Dr. Angiola Borino has been called from Sassari to Perugia.

Dr. Bruno Trambusti has been named professor of pediatrics at Parma.

Dr. Vittorio Zambrina has been named professor of pediatrics at Padua.

Dr. P. Lereboullet, professor of diseases of early childhood, has been promoted to Officer of the Legion of Honor.

Dr. G. C. Bentivoglio has taken charge at Sassari.

CORRECTION

In the article by Dr. Dorothy Engelhard Lane, entitled, "The Nutrition of Twins on a Vegetable Diet During Pregnancy, the Nursing Period and Infancy," which appeared in the December issue (AM. J. DIS. CHILD. **42**:1384, 1931) the first line at the top of page 1385 should read:

"In 1918, McClugage and Mendel,[3] experimenting with dogs, pub-"

Abstracts from Current Literature

Anatomy and Physiology

THE HISTOLOGIC STRUCTURE OF THE CELIAC GANGLIONS IN CHILDREN. V. ZAMORANI, Scritti medici dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 640.

The histologic picture of the celiac ganglions from sections taken from children of various ages (new-born infants to children 2 years old) is described and compared with similar sections from adults. The structure of the ganglions at birth is very incomplete, and although development after birth is quite rapid, maturity is not completely reached by the second year. Considering that incomplete structure means incomplete function, one can easily explain the vagotonia of the infant and the instability of the vegetative nervous system seen in the gastrointestinal disturbances of the nursing child.

HIGGINS, Boston.

EGG ALBUMIN IN HUMAN MILK. P. GYÖRGY, Jahrb. f. Kinderh. **132**:1 (June) 1931.

The author presents an excellent review of the published proofs of the presence of egg albumin in human milk, together with a new proof. Minute quantities of egg albumin added to the serum of a patient with eczema who was sensitive to egg were found to lessen the intensity of the Prausnitz-Küstner reaction produced either by local application or by the ingestion of egg. By this method, the presence of egg albumin was demonstrated in the milk of wet-nurses who partook of raw eggs, but not unless they had, and not in cow's milk.

CLAUSEN, Rochester, N. Y.

IMBIBITION BY FATTY TISSUES. P. C. MALLAM, Ztschr. f. d. ges. exper. Med. **71**:236, 1930.

The amount of water absorbed by pieces of adipose tissue removed from the abdomen post mortem did not depend on the cause of death, and the concentration of the solution in which they were placed had but slight influence. Acid and base both increased the imbibition of distilled water. Lactic acid had the most marked effect; sodium chloride had none; potassium chloride had only a slight effect; calcium chloride produced marked swelling; magnesium chloride inhibited swelling in even very dilute solutions.

KUGELMASS, New York.

THE JUVENILE THORAX. J. BROCK and E. STEMMIER, Ztschr. f. Kinderh. **51**: 322, 1931.

Five hundred and twenty-two normal children from infancy to 13 years of age were studied anthropometrically with especial attention to the thorax. The data give an accurate knowledge of the chest except in very small children, in whom only the chest circumference was measured. In all cases the angle of inclination of the upper aperture was determined by Hofbauer's method, and for the first time averages and limits of variations of this angle are available. The angle shows somewhat the same falling off for age as the relative chest circumference and relative transverse diameter, only the relative sagittal diameter showing a marked diminution. The angle ceases to diminish at the eleventh year and begins to increase, just like the relative chest circumference, apparently to be related to

the stronger development of the inspiratory musculature. After the fourth year, girls have not only a proportionately flatter, thinner and narrower but also a somewhat more depressed chest (a smaller aperture angle) than boys. How far the normal form of the chest is changed by the course of the ribs, especially their gradual sinking, was also studied. To this end, cross and longitudinal sections of the thorax and calculated correlations were considered. As to the first, it appears that the relative sagittal diameter up to the twelfth year is six times more diminished than would be expected from the depression of the ribs. As to the second, the angle of inclination of the ribs (the upper aperture angle), the relative chest depth and the relative chest circumference, in spite of a parallel falling off of their average values with increasing age, vary from one another in marked degree, so that the calculated correlative coefficients are only slightly positive. The chest is not only flatter and narrower, but there are only average values in the different dimensions, according to a certain parallelism of growth. In the children with an asthenic habitus there is usually a reduced aperture angle and depth—indeed, about the same respective values. Both are only relative, for here also the pathologic sinking would shorten the sagittal diameter only about one sixth of the real value. Of clinical interest is the fact that most asthenic children have a flat and sunken chest, but not a narrow one. In many cases of extreme flatness the transverse diameter exceeds the normal. The relative chest circumference in such cases is diminished insignificantly.

EMERSON, Boston.

THE MECHANICAL REGULATION OF HEART TONES IN PREMATURE AND FULL TERM BABIES. W. GANS, Ztschr. f. Kinderh. **51**:409, 1931.

The heart tones and murmurs of sixty children of all ages were registered by means of the oscillograph made by Siemens, and special attention was given to premature and older infants. The similarity between babies and adults was definite, except that the second sound was not so sharp in the very young. The so-called embryocardia of premature infants on accurate analysis is only apparent; there is a shifting of phase between the first and second tones. Congenital heart murmurs show frequencies of from 100 to 200 and may be of lower rate than acquired murmurs, which under some circumstances is of diagnostic value.

EMERSON, Boston.

OSSIFICATION OF THE BONES OF THE HAND: I. PHYSIOLOGIC PROGRESS BY WAVES OF DIFFERENTIATION. RELATION OF FORM OF GROWTH TO DIFFERENTIATION. PROGNOSIS OF BODY SIZE. FIRST METACARPAL. E. STETTNER, Ztschr. f. Kinderh. **51**:435, 1931.

A new hypothesis is presented as to the time of occurrence of the sites of ossification in the bones of the hand in "normal" children, a hypothesis that points out that growth is by fits and starts. In general, the progress of growth in length corresponds to the degree of differentiation, and this relation is definitely valid for certain periods of childhood. Well developed children experience a special increase in the rate of differentiation in the growth of bone as young children and during puberty, but there is almost a standstill between 6 and 10 years of age. The poorly developed have the differentiation retarded up to 10 years of age, but the retardation is made good later. Physiologic conditions make the decision, as between good and bad development, apparently early in childhood. The variation in the time of the appearance of the sites of ossification is very great, notwithstanding the high standards used to pick out "normal" children, and is caused by constitutional peculiarities, the sequence of differentiation and exogenous factors. In the metacarpal bones, the time is regular and the sequence more certain than in the carpal bones.

EMERSON, Boston.

OSSIFICATION OF THE BONES OF THE HAND: II. PSEUDO-EPIPHYSES. E. STETTNER, Ztschr. f. Kinderh. **51**:459, 1931.

On the basis of 2,700 roentgen examinations of the hand (1,843 persons), a study was made of the significance of pseudo-epiphyses. They were associated with the age periods from infancy to puberty, and only in some cases were outside of these limits. For the groups by years, there was a varying high degree of frequency. It could be established that in normal children beyond the age of 1 year and 6 months, pseudo-epiphyses happened in about one third of the cases; in children burdened with disturbances of development, constitutional anomalies and endocrine diseases, principally of the hypophyses, pseudo-epiphyses were noted in two thirds of the cases. It could be concluded that pseudo-epiphyses found in later life pointed to a disturbance of development before birth. Patients with hypersensitiveness of constitutional origin and acquired central ailments showed pseudo-epiphyses with more than average frequency.

EMERSON, Boston.

ACTION OF BLOOD ON URIC ACID. A. ROWINSKA, Acta biol. exper. **6**:37, 1930.

Hemolyzed human or avian blood destroys uric acid. The velocity of decomposition is retarded by a diminution of the oxygen supply. Unhemolyzed blood does not catalyze the oxidation of uric acid.

KUGELMASS, New York.

Pathology, Bacteriology and Biochemistry

DISTRIBUTION OF REAGINS IN THE BLOOD PLASMA. E. L. SHERRER, J. Allergy **2**:467 (Sept.) 1931.

The author's conclusions are as follows: "1. Plasma and serum contain similar amounts of reagin. 2. The albumins and the diffusible portion of the serum contain no reagin. 3. The globulins, particularly the pseudoglobulin, contain all of the reagins. 4. No substance that might inhibit a positive skin reaction has been demonstrated in the serum. 5. The reagins are similar to immune bodies in their association with the globulin fraction."

HOYER, Cincinnati.

BLOOD CALCIUM CHANGES FOLLOWING ADMINISTRATION OF CALCIUM GLUCONATE GIVEN SUBCUTANEOUSLY TO NORMAL AND PARATHYROIDECTOMIZED DOGS AND PER OS TO HUMAN BEINGS. ARNOLD L. LIEBERMAN, J. Pharmacol. & Exper. Therap. **42**:245 (June) 1931.

Calcium gluconate caused a considerable rise in blood calcium in normal and parathyroidectomized animals, reacting a maximum in about an hour and falling to normal in a few hours, more rapidly in the first two hours in the parathyroidectomized animals. Human beings showed a considerable rise in blood calcium with an oral dose of 10 Gm., unless diarrhea resulted; this is likely to occur when the drug is taken on an empty stomach. This preparation has the great advantage of being nonirritant in subcutaneous and intramuscular injections. As it contains but 12.5 per cent calcium (as oxide), larger doses than those of the usual calcium salts are necessary.

PILCHER, Cleveland.

LABORATORY AIDS IN THE DIAGNOSIS OF UNDULANT FEVER. RUTH GILBERT and MARION B. COLEMAN, New York State J. Med. **31**:1087 (Sept. 1) 1931.

As undulant fever is not uncommon in cattle in New York, cases of the disease will continue to be found in districts where raw milk is used. It has been demonstrated that the agglutination reactions with Bacillus abortus and B. melitensis are nearly identical and only one antigen is needed. B. abortus was chosen for use by the State Laboratory. Localized abdominal pain and tenderness due to

undulant fever may lead to mistakes in diagnosis and to unnecessary surgical procedures. Specimens of blood should be obtained during a febrile reaction, and the examinations should be frequently repeated.

AIKMAN, Rochester, N. Y.

FURTHER NOTES ON EXAMINATION OF CEREBRO-SPINAL FLUID BY ULTRA-VIOLET LIGHT. E. F. SKINNER, J. Neurol. & Psychopath. **11**:144 (Oct.) 1930.

A second and more comprehensive study of the absorption of ultraviolet rays by the cerebrospinal fluid is presented. This paper is more valuable and convincing than the first because the usual spinal fluid examinations are recorded in each case along with the spectroscopic picture. A striking observation is that neither the cell count nor the absolute protein content is responsible for the reaction. A case of dementia paralytica in which the pleocytosis and protein are increased to about the same degree as they are in a case of tuberculous meningitis gives thoroughly different spectroscopic features. Skinner feels convinced, therefore, that the absorption depends on some undetermined physical factor in the spinal fluid. He believes that this phenomenon, as well as the colloidal gold curve, depends on similar though not identical variations in the surface charges of particles of colloid. The author concludes that he formerly stressed too much the individuality of the spectrogram in the conditions he studied. The amount of absorption, on the other hand, is much more valuable in reference to recoverability in the cases of meningitis than it is to identify the etiologic type.

BECK, Buffalo [ARCH. NEUROL. & PSYCHIAT.].

CRYSTALLIZATION OF HEMOGLOBIN IN VARIOUS AGES OF LIFE. F. NICOLETTI, Arch. di antropol. crim. **50**:386, 1930.

The author studied the morphologic aspect of the crystals of hemoglobin in relationship to age Hemoglobin crystallizes in the reduced state. Crystallization takes place more promptly in fresh venous blood and coagulated blood than in desiccated blood. The precipitation of crystals in venous or coagulated blood during intra-uterine life begins within from twelve to fourteen hours, and within from twelve to thirty-four hours during extra-uterine life. In desiccated blood, the respective figures are from twenty to twenty-four, and from twenty to seventy-two hours. Morphologically, the crystals have the same aspect whether they are precipitated from fresh, coagulated or desiccated blood. The paramarginal precipitation of crystals on a preparation is always more prompt and more rich than the central. The hemoglobin of the embryo, of the fetus, of the new-born and of infants during the first two or three weeks of life crystallizes in the shape of needles or of fine sharp-pointed rectangular tablets in a flutelike arrangement. The hemoglobin crystals in persons of more advanced age are precipitated almost exclusively in the shape of flat rectangular tablets of larger size. Such tablets are a more developed (mature) form of crystal. It is on their presence or absence that the differential diagnosis of the age of the person may be based. The study of morphology of the crystals of hemoglobin offers, therefore, an application in medicolegal practice.

YAKOVLEV, Palmer, Mass. [ARCH. NEUROL. & PSYCHIAT.].

ACTION OF THE ANTERIOR LOBE OF THE HYPOPHYSIS ON THE METABOLISM OF RESPIRATION AND GLYCOGENESIS IN THE WHITE RAT. A. ARTUNDO and P. MAZZOCCO, Rev. Soc. argent. de biol. **6**:391, 1930.

Studies of Houssay and Biasotti demonstrated that the anterior lobe of the hypophysis plays an important part in the metabolism of the hydrates of carbon. Other authors have pointed out a stimulating action of the hypophysis on the thyroid. An attempt was made by Artundo and Mazzocco to determine the effect

produced by the injection of the fresh anterior lobe of the hypophysis on the metabolism of respiration and on the glycogen content of the muscle and liver. White adult rats were employed. The anterior lobes of three freshly killed rats were suspended in physiologic solution of sodium chloride, and injected intraperitoneally. The respiratory interchange was determined in a respiratory chamber; the rats were then killed, and the dextrose content of the liver, muscles and blood was determined. Only seven rats were used. The results did not warrant any definite conclusions.

HARRISON, Iowa City.

THE EFFECT OF HYPOPHYSEAL EXTRACT (POSTERIOR LOBE) ON WATER METABOLISM. PAUL ROBOZ, Arch. f. exper. Path. u. Pharmakol. **159**:562, 1931.

The urine output and the increase in the water content of the blood in dogs were measured at intervals following the injection of Ringer's solution, the injection of Ringer's solution and hypophyseal extract and the injection of varying amounts of hypophyseal extract. It was found that the extract did not increase the water-binding power of the tissues, so that interference with diuresis depended on an action of the extract on the kidney alone. There was, moreover, a definite increase in the water content of the blood, which depended not only on the failure of the kidneys to excrete, but also on an addition to the blood stream of water withdrawn from the tissues. A detailed analysis of the effect of hypophyseal extract on the hydremia shows the following additional facts: 1. After small doses of the extract there is an immediate diuresis, with a slight hydremia. 2. After large doses the diuresis is, for the most part, diminished, and there is a high grade hydremia. 3. After large doses there is a later period at which time the diuresis is increased. Insulin affects the hypophyseal hydremia antagonistically.

LESLIE, Evanston, Ill.

THE NORMAL CONSTITUTION OF THE BLOOD IN CHILDHOOD. EUGEN STRANSKY, Kinderärztl. Praxis **2**:136 (March) 1931.

Stransky presents a detailed account of the hemoglobin, erythrocytes, leukocytes and differential blood counts in premature, new-born and older infants and children.

HUENEKENS, Minneapolis.

DEPOSITIONS OF FAT IN THE LIVER AND THE CORTEX OF THE SUPRARENAL GLAND IN INFANTS AND CHILDREN. P. ROSENBAUM, Ztschr. f. Kinderh. **51**:70 (May) 1931.

Removal of fat from the cortex of the suprarenal gland and fatty degeneration of the liver cells not only are connected with the kind of disease and etiologic agent, but are related to each other. They run parallel, without any question. Great significance is attached to the kind of etiologic agent; e. g., staphylococcic infections leave the fat content uninfluenced; pneumococcic and streptococcic infections influence fat metabolism greatly.

EMERSON, Boston.

GAS EXCHANGE IN RUNNING. K. IMAMURA and F. MATSUDA, J. Pediat. (Tokyo), July 20, 1931, no. 374, p. 1003.

The authors made determinations of the gas exchange in twenty-three boys about 12 or 13 years of age. They were required to run for a distance of 50, 100 and 200 meters, two and one-half hours after a meal. The determinations were made just before, immediately after, thirty minutes after and one hour after running, by means of the Knipping apparatus. It was found that immediately after running, the rate of gas exchange is greatly increased; namely, the value was 0.83 before running, 1.039 immediately after running 50 meters, 1.099 after 100 meters and 1.174 after 200 meters. The oxygen consumption was nearly twice as

much as that before running. There was a rise in the respiratory quotient, due to the rise in the value of carbon dioxide. Thirty minutes after running, there was still a high oxygen consumption value, but the carbon dioxide rapidly decreased, so that the respiratory quotient fell even below the normal value. After one hour, the normal values were usually reached. Thus, from the standpoint of gas exchange studies, running distances up to 200 meters is a beneficial exercise for children of this age.

KATO, Chicago.

AGE VARIATIONS IN ACID-BASE EQUILIBRIUM IN NORMAL AND STARVED RABBITS. A. KOBAYASHI, J. Pediat. (Tokyo), July 20, 1931, no. 374, p. 1042.

The author finds that in normal rabbits the average value for the blood p_H tends to go to the side of acidity most markedly in the last stage of prenatal life, but no noticeable variations are found in the animals after birth up to 7 weeks of age. The average carbon dioxide value is high during the first twenty days of life; it is lowest in prenatal life. There is no variation worthy of special mention in these values in starved animals.

KATO, Chicago.

Nutrition

EXPERIMENTAL RICKETS AND CALCIFICATION OF DENTIN. H. BECKS and W. B. RYDER, Arch. Path. **12**:358 (Sept.) 1931.

In the course of a histologic study of the changes in the teeth of growing rats that had been placed on a rachitogenic diet, the authors made the following observations: There is a diminution in the amount of calcium salts deposited in the dentin, even after so short a period as seven days. There is a change in the type of calcification from a homogeneous to an irregular globular type and a widening of the dentinoid matrix. Atrophy of the odontoblasts appears after fourteen days. It is believed that this is a primary cellular atrophy developing after the cellular vitamin D has been utilized. In the same sections, an arrest of calcification may be observed in relation to atrophic odontoblasts, with the continued deposition of lime salts by adjacent vital odontoblasts. For this reason, the authors believe that rachitic manifestations in the teeth and bones are due to injury to the odontoblasts and osteoblasts from lack of vitamin D, rather than to an insufficient supply of calcium and phosphorus. In conclusion, they state that "the odontoblasts are chiefly responsible for the formation of dentin. They are required to produce the cementing substance which holds von Korff's fibers in place. Their presence is necessary to form Tomes' processes and so give nutrition and calcifying material to the dentin, and furthermore in order that calcium salts may be deposited and the matrix calcified." The article is well illustrated.

LESLIE, Evanston, Ill.

A STUDY OF THE PROPHYLACTIC VALUE OF VARIOUS ANTIRACHITIC AGENTS. ADOLPH G. DE SANCTIS and JOHN DORSEY CRAIG, Arch. Pediat. **48**:595 (Sept.) 1931.

"This clinical study was undertaken to determine the prophylactic value of various antirachitic agents in infants rather than in experimental animals. . . . In this clinical study, the infants have been divided into several groups:

"Group 1. Those given cod liver oil—3 teaspoonfuls daily or
(1400-1700 Oslo rat units)
(140-170 Steenbock rat units)

"Group 2. Those given irradiated ergosterol 100 D—10 drops a day.

"Group 3. Those given irradiated ergosterol 250 D—10 drops a day
(7500 Oslo rat units)
(750 Steenbock rat units)

"Group 4. Those given irradiated ergosterol 500 D—10 drops a day
(15000 Oslo rat units)
(1500 Steenbock rat units)

"Group 5. Those given cod liver oil concentrate in tablet form, three tablets a day
(1500 Oslo rat units)
(150 Steenbock rat units)

"It will be noted that all infants in Groups 2, 3 and 4 received more units of D than those in the 1st and 5th groups (cod liver oil and cod concentrate); that those on 100 D viosterol received twice as many D units and those on 250 D, and 500 D irradiated ergosterol received five and ten times as much vitamin D respectively as those on cod liver oil. It is important that this be remembered in comparing results."

The authors include as clinical evidence of rickets marked occipital craniotabes, moderate or marked costochondral beading, grooving and flaring of the ribs, epiphyseal enlargement and spasmophilia. The cases studied were all similar as to the age of the infant, the duration of time of the experiment, the dietary treatment and the rate of growth. Tables are included showing the comparative value of agents used and types of feeding.

The conclusions were: "1. Cod liver oil in a dosage of three teaspoonfuls a day (about 170 Steenbock vitamin D units) prevented rickets in 97 per cent of 100 cases studied. 2. Viosterol 100 D, given in 10 drop daily doses (300 Steenbock units), prevented rickets in 77 per cent of the cases studied. 3. Viosterol 250 D, given in 10 drop daily doses (300 Steenbock vitamin D units), prevented rickets in 81 per cent of the cases studied. 4. Viosterol 500 D, given in 10 drop doses (1500 Steenbock vitamin D units), prevented rickets in 90 per cent of the cases studied. 5. Cod liver oil in concentrate tablet form, given in doses of three tablets daily (150 Steenbock vitamin D units), prevented rickets in 92½ per cent of the cases studied.

"From the above observations, we note that in the form of cod liver oil in oil form only 170 units of vitamin D are necessary to protect the infant against rickets; in the tablet concentrate form, as many D units are needed, whereas when viosterol is given even 10 times the number of D units does not confer the same immunity against rickets. If rickets is solely a problem of vitamin D deficiency, why is it necessary to give so much more in its pure form (viosterol D only) than when cod liver oil is given? As expressed by us in 1930, we still are of the opinion that rickets is not due to a deficiency of vitamin D alone but that vitamin A and possibly other factors play an important part in this disease."

WADDELL, University, Va.,

VITAMINS IN CANNED FOODS: X. THE VITAMIN CONTENT OF SOME COMMON VEGETABLES. E. F. KOHMAN, W. H. EDDY and CELIA Z. GURIN, Indust. & Engin. Chem. **23**:808, 1931.

Feeding experiments with rats showed that 25 mg. of canned turnip greens supplied approximately as much vitamin A as 5 Gm. of bleached celery and 500 mg. of green celery. Head lettuce appeared to contain more of the vitamin B complex than either celery or canned turnip greens. Head lettuce, celery (bleached and green) and raw carrots were not found to be good sources of vitamin C for guinea-pigs. From 2 to 4 Gm. of canned turnips gave better growth and less evidence of scurvy than 5 Gm. of celery, from 10 to 15 Gm. of head lettuce or 10 Gm. of whole carrots fed daily. Shredding the carrots and withholding them for from one to three hours diminished the amount of vitamin C.

KUGELMASS, New York.

ANTIRACHITIC POTENCY OF THE MILK OF COWS FED IRRADIATED YEAST OR ERGOSTEROL. A. F. HESS, J. M. LEWIS, F. L. MACLEOD and B. H. THOMAS, J. A. M. A. **97**:370 (Aug. 8) 1931.

Viosterol or irradiated yeast supplements to fodder rendered cow's milk highly antirachitic. Given to young infants during the winter, this milk prevented all but the minor rachitic manifestations; rickets evident roentgenologically did not develop, and in those with rickets calcification was brought about in one month. Irradiated yeast produced a more potent milk than ergosterol. The advantage of such milk is that it functions automatically without the necessity of maternal cooperation. The possible danger of overdosage and the danger of commercial exploitation of such milks were pointed out in the discussion, which likewise brought out the fact that there is still an unfathomed factor in regard to the etiology of rickets.

BONAR, Salt Lake City.

THE CURE OF INFANTILE RICKETS WITH TUNGSTEN-FILAMENT RADIATION. H. J. GERSTENBERGER and A. J. HORESH, J. A. M. A. **97**:766 (Sept. 12) 1931.

Three infants with moderately severe rickets were cured by daily twelve hour exposures to suberythema doses of tungsten-filament radiation produced by a 500 watt CX Mazda lamp suspended at a distance of 5½ feet (167.6 cm.). A fourth infant was cured of moderately severe rickets in seven and one-half weeks by one and one-half hour exposures daily at 80 cm.

BONAR, Salt Lake City.

FURTHER INVESTIGATION OF QUANTITATIVE MEASUREMENT OF VITAMIN A VALUES. H. C. SHERMAN and E. L. BATCHELDER, J. Biol. Chem. **91**:505 (May) 1931.

Using for the measurement of vitamin A values, the general method described in previous papers . . . with all added precautions of technic and interpretation suggested by recent advances in our knowledge of the vitamins, we have found that graded increments in the amounts of this vitamin, fed in the form of whole milk powder, cause increases in survival (at low levels of feeding) and in rate of gain in weight (at higher levels) which are relatively greater than have been shown in previously published work. Simple statistical analysis of the experimental results indicates that, at levels of feeding which induce a gain in weight of about 3 Gm. per week, a decrease of 25 per cent (or an increase of 33 per cent) is undoubtedly measurable by the method here used when nine or more carefully standardized experimental animals are employed at each level of feeding.

AUTHORS' SUMMARY.

FAT-SOLUBLE VITAMIN: XXXIII. DETERMINATION OF VITAMIN A AND ITS STABILITY IN BUTTER FAT TO ULTRA-VIOLET RADIATIONS. H. STEENBOCK and ALICE M. WIRICK, J. Dairy Sc. **14**:229, 1931.

Butter fat irradiated for periods of from thirty to one hundred and twenty minutes at depths varying from 0.08 to 0.64 cm. was fed at different intake levels to experimental rats. The basal ration was composed of purified casein 18 per cent, agar 2 per cent, salts 4 per cents, yeast 8 per cent and starch 68 per cent, and was irradiated. This diet was antirachitically active, but lacked vitamin A. When it was fed to experimental rats, ophthalmia developed in five weeks, and at this time curative quantities of irradiated butter fat were added to the diet. The destruction of vitamin A was proportional to the time of irradiation and inversely proportional to the thickness of the layer of fat exposed. A series of experiments was used to determine whether the Evans-Bishop method of using a vaginal smear had any advantages over the reinitiation of growth or the cure of ophthalmia.

The latter method was preferred. Another series of experiments showed that destruction of vitamin A is retarded when irradiation is carried out in an atmosphere of carbon dioxide, nitrogen and hydrogen. Butter fat, antirachitically activated, retained most of its vitamin A after seven months' storage at room temperature.

KUGELMASS, New York.

DIETARY FACTORS INFLUENCING CALCIUM ASSIMILATION: XIV. THE INFLUENCE OF MINERAL ACIDS AND SUGAR ON THE CALCIUM METABOLISM OF MILKING COWS. E. B. HART, H. STEENBOCK, O. L. KLINE and G. C. HUMPHREY, J. Diary Sc. **14**:307, 1931.

The addition of 3 pounds (1.3 Kg.) of dextrose to a daily ration of hay, ensilage, cereal grains and cereal grain concentrate did not consistently influence the calcium assimilation of milking cows. The daily addition of 115 or 230 cc. of 40 per cent hydrochloric acid increased the calcium excretion in the urine with a greater net loss to the animal than when no acid was fed. The use of this acid affected the p_H value of the milk. The experiments did not aid in indicating the factor in green plant tissue that promotes the utilization of calcium.

KUGELMASS, New York.

CALCIUM AND PHOSPHORUS BALANCES OF MILKING COWS UNDER VARYING CONDITIONS. H. B. ELLENBERGER and J. A. NEWLANDER, Proc. Am. Soc. Animal Production, 1928, p. 25.

Results of experiments extending over a period of several years show that liberally milked cows are not always in serious negative balance as regards calcium and phosphorus, even when receiving comparatively little or no leguminous roughage, provided they are fed liberal amounts of a well balanced supplementary grain mixture. Added minerals in the form of steamed bone meal and finely ground limestone may be assimilated in sufficient quantities to result in appreciable positive balances of calcium and phosphorus, but the addition of mineral supplements does not necessarily improve rations for cows kept on farms in the northeastern part of the United States.

KUGELMASS, New York.

THE ANTIRACHITIC POTENCY OF COD-LIVER OIL WHEN MIXED AND STORED IN FEED SIX AND TWELVE MONTHS. LOYAL F. PAYNE, Proc. Fourth World's Poultry Congress (London), 1930, p. 316.

A good grade of tested cod liver oil was added to two lots of specially prepared feed mixtures for storage, and a sample of oil was set aside to be added to a similar feed mixture at the time the mixed lots were fed to chicks. The feed mixed with cod liver oil was fed (*a*) immediately after mixing, (*b*) after storage for six months and (*c*) after storage for twelve months. After six and twelve months freshly mixed oil and feed and previously mixed and stored oil and feed were fed. Analyses were made of the calcium and phosphorus in the blood and of the ash in the tibia and femur. One per cent of cod liver oil stored in feed for one year was found to retain its antirachitic potency when tested by feeding the chicks for eight weeks. Five per cent of the mineral mixture, consisting of two parts steamed bone meal, two parts calcium carbonate and 1 part sodium chloride added to the same basal ration prevented rickets in the absence of vitamin D under similar conditions.

KUGELMASS, New York.

THE INFLUENCE OF THE PROTEIN LEVEL ON THE RATE OF GROWTH IN CHICKENS. G. F. HEUSER and L. C. NORRIS, Proc. Fourth World's Poultry Congress (London), 1930, p. 328.

Protein levels in rations for chicks were varied from approximately 13 to 20 per cent. Chicks on the higher levels of protein grew more rapidly up to 10 weeks of age, whereas those on lower levels of protein grew more rapidly thereafter.

The ultimate weight of the chicks at 20 weeks was approximately the same. To obtain early rapid growth the ration should contain at least 20 per cent of protein during the first six to eight weeks, 18 per cent from the twelfth to the fourteenth week and from 15 to 16 per cent to the end of the growing period.

KUGELMASS, New York.

CONGENITAL ATONIA, HYPOCALCEMIA: REMARKABLE IMPROVEMENT WITH LARGE DOSES OF VIOSTEROL. L. RIBADEAU-DUMAS, BOURGUIGNON and MAX LÉVY, Bull. Soc. de pédiat. de Paris **29**:110 (Feb.) 1931.

A female infant, 18 months old, poorly developed and poorly nourished, showed marked hypotonicity of all the muscles and marked mental retardation. She made little improvement under a proper dietary regimen, supplemented by ultraviolet irradiation and 20 drops of viosterol daily. The blood calcium was found to be low, 7.88 mg. per hundred cubic centimeters. She was then given 4 cc. of viosterol over a period of forty-four days, with marked improvement. The blood calcium rose to 13.1 mg. per hundred cubic centimeters. With the withdrawal of the viosterol the child returned to her previous condition.

BENJAMIN, Montreal, Canada.

DEHYDRATION FEVER. A. B. MARFAN, Nourrisson **19**:260 (July) 1931.

Others have described the appearance of fever in infants fed on dilutions of dried milk. Finkelstein believed that such fever is due to an abnormal ration between the protein and the quantity of water in which it is dissolved. If sodium chloride or urea is also given in too concentrated a solution, fever results. Withholding water alone does not produce fever. On the basis of a disturbed water balance (protein, sodium, chloride, urea), Finkelstein designated these particular substances as hydrophiles. Their metabolism requires a certain quantity of water. If this is not supplied through the gastro-intestinal tract or parenterally, it must be obtained from the tissues. This results in dehydration, which in turn causes the fever. He argued also that the fever accompanying the gastro-intestinal disturbances in infants can also be explained on the basis of a disturbed water balance. Marfan does not believe that the foregoing explanations can be accepted without further study and observation.

MCCLELLAND, Cleveland.

EXPERIMENTAL RESEARCH ON THE ACTION OF IRRADIATED ERGOSTEROL. H. SIMONNET and G. TANRET, Presse méd. **39**:932 (June 24) 1931.

A tremendous amount of work has been done on the action of irradiated ergosterol, and this article is simply a résumé of the personal conclusions of the authors. Viosterol is a complex mixture of the products of transformation of ergosterol by ultraviolet irradiation. The unit of measure proposed by Lesne and Clement is practical. It is: "The smallest amount that will protect a young white rat weighing 40 Gm. for fifteen days against rickets."

Ergosterol is toxic in large doses and produces untoward calcification, but even the most harmless drug cannot be given in unlimited quantities without ill effects. Too prolonged irradiation not only destroys the vitamin, but increases the toxicity of the drug. Animals vary greatly in their response to ergosterol; the cat is most sensitive, the monkey the least so. Antirachitic potency, contrary to previous views, is very resistant to time, temperature, oxidation and reduction.

The toxic and calcifying properties are separate and distinct. An animal may survive extensive calcification; another may become toxic and die with no calcification whatever. Some animals exhibit a surprising resistance to ergosterol, comparable to the insulin resistance of certain animals. In slow calcification, the source of calcium is ingested food, but when calcification is extremely rapid, decalcification of bones takes place. The rapid mobilization of calcium in diseased

lung tissue occurs when tuberculous rabbits are given ergosterol. When pregnant rats were given ergosterol, the young showed remarkable resistance to rickets, even when placed on a rachitogenic diet.

BIEKER, St. Petersburg, Fla.

SULPHUR AND GROWTH. L. BINET and A. ARNAUDET, Presse méd. **39**:1120 (July 25) 1931.

The presence of a much larger amount of sulphur in young subjects than in those in whom full growth has been attained suggests that sulphur may have some bearing on growth. It occurs principally as glutathione, a dipeptide formed by the union of a molecule of cysteine with one of glutamic acid. It occurs in some forms of life only at the time of division of the egg; in some it diminishes rapidly as cellular division is accomplished. This fact points to some bearing on growth, and it is logical to conclude that some sulphur might well be included in the dietary of the growing animal or child.

BIEKER, St. Petersburg, Fla.

THE NECESSITY OF ADOPTING AN INTERNATIONAL ANTIRACHITIC UNIT FOR THE DOSAGE OF VITAMIN D (IRRADIATED ERGOSTEROL). G. TIXIER, Presse méd. **39**:1187 (Aug. 8) 1931.

Of a number of proposed antirachitic units of irradiated viosterol only two are practical, the biologic and the physiologic. These are often confused, with regrettable errors in dosage. It is important that an international unit be adopted to serve as a basis for the dosage. For determining the unit, the white rat is the animal of choice. It should be kept in a room of even temperature (28 C.). Diet 3143 of MacCallum is suggested, with a test period of eighteen days and roentgenograms of the knee as a means of control.

BIEKER, St. Petersburg, Fla.

THE UNRECOGNIZED DYSTROPHIES. GEORGES MOURIQUAND, Presse méd. **39**: 1373 (Sept. 19) 1931.

Mouriquand states that all dystrophies imply a disturbance of nutritional equilibrium. The dystrophies of alimentary origin may be classified as (1) quantitative, (2) qualitative and (3) mixed. The first type results from overfeeding or underfeeding, as the name implies. The second is concerned with lack of balance in food, either in definite chemical substances or in the vitamins. The third type is frequently found as a combination of overfeeding or underfeeding, deficiency and improper balance. The paper is chiefly concerned with the results of vitamin deficiency. The frank manifestation of a deficient diet are well known, but too often the atypical cases and the "predeficiency" stage are unrecognized. These may be manifested by a lowered resistance to infection and by subacute or chronic digestive troubles, or they may be entirely unsuspected until some crisis suddenly reveals their presence.

BIEKER, St. Petersburg, Fla.

ACTION OF ULTRAVIOLET RAYS AND OF IRRADIATED ERGOSTEROL IN RACHITIS WITH SPECIAL REGARD TO THE BEHAVIOR OF THE PHOSPHORUS AND CALCIUM LEVEL IN THE BLOOD AND CEREBROSPINAL FLUID. A. MACCHI, Pediatria **37**:1175, 1929.

In the first series of experiments from 5 to 6 mg. of viosterol per day was administered to babies every other day, while in the second series the babies were exposed to ultraviolet irradiation on alternating days. In both series calcium and phosphorus were estimated in the serum and cerebrospinal fluid every ten days; at the same time a roentgen examination of the bones was made. The initial calcium in the cerebrospinal fluid (from 5.6 to 7.3) and especially in the serum (from 10.1 to 12.6) was higher than normal, while the initial phosphorus (from 1.22 to 1.94 and from 3.06 to 4.54, respectively) was below normal. When serum from

rachitic children was irradiated in vitro for fifteen minutes at a distance of 60 cm., a considerable increase of phosphorus occurred. Either no change or only slight changes were seen after the irradiation of serum from cured rachitic children. The modification of the phosphorus and calcium level observed in the course of the treatments are assumed to be connected with the action of vitamin D.

KUGELMASS, New York.

EXPERIMENTAL RICKETS IN THE RAT: V. ON THE TOXICITY OF IRRADIATED ERGOSTEROL. P. GYÖRGY and G. POPOVICIU, Jahrb. f. Kinderh. **132**:34 (June) 1931.

After a full discussion of the literature on the toxicity of irradiated ergosterol, the authors describe a technic for estimating this toxicity by using mice fed a standard normal diet. It is shown that the toxic dose bears a definite relationship, within the limits of error of the method, to the dose required to prevent rickets in the rat; this relationship (the "therapeutic index") varies from 10,000 to 50,000. By the heating of irradiated ergosterol to 200 C., the antirachitic potency is diminished from 1,000 to 10,000 times, while the toxicity changes but little. Such heated preparations no longer raise the serum phosphate or calcium of rats with "low phosphate" or "low calcium" rickets, but may still cause elevation of these values (and pathologic calcification) in normal rats. Therefore, normal animals may not be used for the assay of antirachitic agents. Irradiated ergosterol, freed from unchanged sterol by means of digitonin and inactivated by heat, may be reactivated by ultraviolet irradiation. This fact tends to support the idea that the toxicity and antirachitic effect depend on one labile substance. By repeated heating and irradiation, it was not possible to increase the therapeutic index.

CLAUSEN, Rochester, N. Y.

THERAPY AND PROPHYLAXIS OF RICKETS. KARL SCHMITT, Kinderärztl. Praxis **2**:119 (March) 1931.

On theoretical and practical grounds the author doubts the efficacy of viosterol in the prophylaxis and treatment of rickets. He recommends a carefully standardized cod liver oil to which viosterol has been added.

HUENEKENS, Minneapolis.

TREATMENT OF RICKETS AND SPASMOPHILIA WITH A MILD POWDERED VIOSTEROL. W. CATEL, Monatschr. f. Kinderh. **51**:81 (Oct.) 1931.

In the Children's Clinic at Leipzig, whole milk plus rice powder has been used as a feeding for infants. The use of whole milk plus the carbohydrate addition did not lead to diarrheal disease, but, on the other hand, the feeding did not prevent rickets. A number of expedients were used, such as the addition of egg yolk and also viosterol, but practical difficulties stood in the way. Finally it was found that viosterol could be prepared in powdered form by a certain pharmaceutical house. The addition of this preparation to the whole milk rice mixtures was a satisfactory method of preventing rickets. The cases were controlled by means of roentgenograms and examinations for blood phosphorus.

GERSTLEY, Chicago.

EXPERIMENTAL ERGOSTEROL POISONING. M. HAENDEL and J. MALET, Virchows Arch. f. path. Anat. **276**:1, 1930.

The administration of irradiated ergosterol to rabbits and guinea-pigs caused cachexia, which was associated with cholesteremia and with lipoid infiltration of the organs. The tissue changes were more marked in castrated than in normal animals. The toxic action of irradiated ergosterol is the same as that of cholesterol.

W. SAPHIR [ARCH. PATH.]

THE PREVENTION OF RICKETS WITH IRRADIATED MILK. K. REICHHUBER, Wien. klin. Wchnschr. **44**:765 (June 12) 1931.

K. Reichhuber concludes that irradiated milk is entirely harmless and does not possess the danger inherent in ergosterol poisoning or that of scurvy through lack of vitamin C. The prophylactic application of this method is trustworthy, and it will become applicable in general when physicians, social agencies and a large dairy company combine their efforts to produce such a product for general consumption.

A. F. ABT, Chicago.

QUANTITATIVE ESTIMATIONS OF THE AMOUNTS OF NATURAL VITAMINS IN FOODS. P. REYHER, Ztschr. f. Ernähr. **1**:81 (March) 1931.

Reyher objects to the loose designation of the vitamin content of nutritional substances in terms of one plus, two plus, etc. He proposes to record in some quantitative and standard form the vitamin content of various foods. In animal experiments he prefers 50 Gm. rats or 250 Gm. pigeons for the study of the vitamin B content and 250 Gm. guinea-pigs for the study of the vitamin C content. He utilized a constant, basic diet dependent on a weighed amount of the food under investigation, as the only source of the vitamin in question. A graphic comparison of various foods was then made in terms of the number of days that given weights protected the animals. The constancy of results at various levels was clearly shown.

WEYMULLER, Brooklyn.

THE CONDITION OF THE SOFT PARTS IN MASS DURING OPEN-AIR TREATMENT OF CHILDREN WITH INACTIVE TUBERCULOSIS. W. KORNFELD and H. SCHÜLLER, Ztschr. f. Kinderh. **51**:349, 1931.

In 160 children being treated for inactive tuberculosis in the open air, measurements were taken at the beginning and at the end of their stay, and the demonstrable changes in the mass of the soft parts were brought into relation with the increase of weight. It was shown that with an increase in weight, the soft parts, with the exception of the lower part of the leg, showed in general a definite increase. Of the four skin areas studied, the abdominal skin had a predilection for the early deposition of fat, in girls more regularly than in boys. The smallest changes were shown by the soft portions of the lower parts of the leg, where there was a transient mild weakening of the musculature because the child was prevented from moving about, for the sake of gaining in weight.

EMERSON, Boston.

THE DURABILITY OF THE GAIN IN WEIGHT OF CHILDREN AFTER OPEN-AIR TREATMENT FOR TUBERCULOSIS. H. HOLZER and W. KORNFELD, Ztschr. f. Kinderh. **51**:363, 1931.

In 146 children who were given open-air treatment because they had inactive tuberculosis and were underweight, or because of a poor appearance, some of them in the roof ward of the Children's Hospital in Vienna and others in the convalescent ward in Wiedlingau-Wurzbachtal, the increase in weight was followed for a long time after discharge. At the time of treatment, for a similar stay in the hospital and a similar age period, the gain at Weidlingau amounted to 4.3 Kg.; in the roof ward, 3.2 Kg. From two to four months after discharge, the children from Weidlingau had lost 0.9 Kg., whereas those from the roof ward had gained 0.3 Kg. From five to eight months after discharge, the children from the roof ward had gained 0.7 Kg. and the children from Weidlingau had lost 0.8 Kg. One and one-fourth years after discharge, the children from the roof ward had gained 2.8 Kg. and the children from Weidlingau 1.4 Kg. The marked gain in weight of the children while at Weidlingau was balanced by the continuing loss after discharge and the late setting-in of the fresh gain. The loss in weight was the greater, the greater the gain while under treatment. The relative weight at the

beginning of the treatment had but little influence on the weight after cessation of treatment; on the other hand, the weight at the end of treatment had considerable influence on the further course of the weight curve. In girls, corresponding to the great tendency to a precipitate deposition of fat at the time of treatment, the loss of weight was great and rapid after the return to home conditions. The influence that the age of the children had on their readiness to gain under treatment had no counterpart after discharge; the increase was much better maintained in the older children than in the younger ones. On the other hand, small children had a secondary loss of weight which lasted rather long; the large children a gain of weight setting in rather early. These facts were not to be expected with regard to the influence of the constitutional type of body structure; they may have been deceptive because of the small number of cases. The several weight curves showed that the permanence of the increase in weight varied.

EMERSON, Boston.

THE STATE OF THE SOFT PARTS IN CHILDREN AFTER DISCHARGE FROM THE OPEN-AIR TREATMENT. W. KORNFELD and D. OROSZ, Ztschr. f. Kinderh. **51**:381, 1931.

The soft parts and the changes in their mass, with changes in the weight curve, were studied for a long time in sixty-six children who had been treated in the open air at the Children's Clinic in Vienna on account of inactive tuberculosis and a poor general condition. It appeared in general that after discharge a diminution of the soft parts occurred, a diminution that was of unlike degree and duration. It happened often in cases in which the weight fell off a little or even went up. The inequality of the soft parts that resulted from forced feeding gave place to a more regular distribution of fat corresponding to the constitutional type of body, and the fat bolsters in the abdominal skin disappeared. The weight increase that set in some time after discharge was not accompanied again by great and irregular amounts of fat, which characterize quick deposition in the soft parts. Keeping the skin thickness and the mass of the upper part of the arm and the lower part of the leg under observation gave more data as to the weight curve in forced feeding and after convalescent treatment.

EMERSON, Boston.

THE USE OF MILK COAGULATED WITH RENNIN IN THE FEEDING OF BABIES. U. GRÜNINGER and C. HÜNERMANN, Ztschr. f. Kinderh. **51**:419, 1931.

In the feeding of 130 babies on milk coagulated with rennin it was found that such milk is indicated in dystrophy and atrophy, in loss of appetite without fever or disturbance in nutrition, in pylorospasm and in some forms of mild parenteral dyspepsia. The preparation is simple and the cost low.

EMERSON, Boston.

THE METABOLISM OF CREATINE IN PREMATURE PUBERTY. H. FASOLD, Ztschr. f. Kinderh. **51**:527, 1931.

The metabolism of creatine stands in close relation to the maturity of the sexual glands. The adult has no, or almost no, endogenous creatinuria, and uses exogenous creatine quantitatively. Only after large doses does creatinuria appear. The child has a considerable endogenous creatinuria before puberty, and even excretes a small quantity of exogenous creatine. The behavior of creatine metabolism in regard to exogenous creatine was tested in two cases of premature puberty, and new evidence was obtained that the end of infantile exogenous creatinuria is connected with the beginning of the function of the sexual glands. In a girl 8 years old who had menstruated, added creatine was used as in the case of adults. A boy 5 years old who showed signs of premature puberty but had infantile testes, showed the characteristics of juvenile metabolism, an inability to break down creatine. The use of large quantities of ovarian hormone in an 8 year old girl did not influence juvenile creatinuria.

EMERSON, Boston.

Sodium Chloride Acidosis in Infancy. H. Fasold, Ztschr. f. Kinderh. **51**:541, 1931.

Fasold studied the acidotic action of sodium chloride in two babies in the normal and in the acidotic condition of metabolism. The course was entirely different. In the first case there was considerable alkaluria; the excretion of organic acids diminished, the ammonia output increased. Sodium chloride acidosis showed two phases: compensatory excretion of alkali and restitution of the ammonia output. In the urine there was a pseudo-alkalosis. Under acid conditions, on the other hand, there was almost no influence on the acid-base equilibrium; the phosphoric acid was only moderately increased, leaving the increased ammonia output to show that acidosis was present. As an explanation of this situation, the hypothesis is set up that alkali in the tissues was mobilized to intermediary compensation. From these results, which show the acidotic action of sodium chloride, the conclusion is drawn that infusions of sodium chloride or Ringer's solution in intoxication and exsiccation are not indicated, since they increase the acidosis already present. Bicarbonate, as recommended and used with success by Marriott, should be substituted.

Emerson, Boston.

Kefir as an Infant Diet Material. Cenek Saitz, Časop. lék. česk. **68**: 1135 (Aug. 9) 1929.

The history of sour milk feeding up to date is reviewed. The advantages of raw and boiled kefir are given. These include simplicity, conservation of the milk supply, low cost, advantageous quality, digestibility and low rate of putrefaction. In the raw state the presence of an active ferment and a beneficial action on the intestinal flora are cited. The fine flocculent precipitation of the milk proteins is also an advantage.

Stulik, Chicago.

Acid Milks in Infant Feeding. Cenek Saitz, Časop. lék. česk. **68**:1205 (Aug. 30) 1929.

The literature on the use of lactic acid in feeding is reviewed, beginning with the contribution of Lesage in 1886, who reported the use of doses of from 15 to 20 Gm. a day without toxic effects. The well known advantages of lactic acid milk are cited. Hydrochloric acid and acetic acid milks are discussed; there is no advantage of either over lactic acid milk. Vinegar milk is not recommended because of the variability of commercial vinegar and acetic acid. The authors fed 455 infants of various ages lemon juice milk, and recommend its use in mixed feeding during the first three months, and as an artificial diet only in the older infant. Its advantage over lactic acid milk is mainly the presence of vitamin.

Stulik, Chicago.

Prenatal Conditions

Double Monsters: Study of Their Circulatory System and Some Other Anatomical Abnormalities and the Complications in Labor. A. L. Mudaliar, J. Obst. & Gynæc. Brit. Emp. **37**:753, 1930.

The author describes certain obstetric and anatomic features of nine double monsters collected at the Museum of the Giffard School of Obstetrics, Madras. He attended the delivery in four of the cases that took place among 25,000 deliveries. The specimens which he describes consisted of: (1) three cases of thoracopagus tetrabrachius tetrapus, (2) two cases of thoracopagus tribrachius dipus, (3) an anencephalic thoracopagus dibrachius dipus, (4) a syncephalic thoracopagus tetrabrachius tetrapus, (5) a craniopagus and (6) an ischiopagus. Labor is apt to be complicated, though spontaneous delivery has occurred with living twins. They may survive and live many years. In modern practice the antenatal

diagnosis may be made ante partum, especially by the use of the roentgen rays. Cesarean section may be indicated, and in case of survival, after careful study, an operation for surgical separation may be undertaken, if the related anatomic structures make it feasible.

ADAIR, Chicago.

DYSTOCIA DUE TO IDIOPATHIC DILATATION OF FETAL URINARY TRACT. KATHLEEN EDGECOMBE, J. Obst. & Gynæc. Brit. Emp. **37**:832, 1930.

The author describes a fetus born to a 36 year old primipara after a normal pregnancy. The head was delivered by forceps, but the body could not be extracted. A diagnosis of fetal ascites was made; the abdomen was punctured and fluid withdrawn. The fetus weighed 6½ pounds (2.9 Kg.), was 19½ inches (49.5 cm.) long and measured 18 inches (45.7 cm.) in circumference at the umbilicus. The bladder was dilated, as were the ureters and kidney pelvis. The right kidney was cystic. No obstruction was found in the urinary tract. The other organs and structures seemed normal, except that there was a persistence of the primitive cloaca, with an imperforate anus.

ADAIR, Chicago.

THE PULMONARY ARTERY IMPRESSION ON THE OESOPHAGUS. JOHN PARKINSON and D. EVAN BEDFORD, Lancet **2**:337 (Aug. 15) 1931.

Roentgenoscopy of the esophagus after the introduction of barium sulphate has proved helpful in the investigation of disease of the esophagus, and the authors point out how it may be of help in investigating abnormalities of the pulmonary artery as well. In many congenital malformations of the heart, the pulmonary artery is enlarged, perhaps most commonly in association with patent ductus arteriosus. In general, the size of the pulmonary artery varies inversely with that of the aorta; when the artery is large, the aorta is usually small. The authors' roentgen observations with the barium sulphate method support this fact.

LANGMANN, New York.

CONGENITAL ELEVATION OF THE DIAPHRAGM. W. BURTON WOOD and FRANKLIN G. WOOD, Lancet **2**:392 (Aug. 22) 1931.

Congenital elevation of the diaphragm is a condition due to faulty development of this organ, as the result of which the diaphragmatic dome on one side, usually the left, forms a sac bulging upward into the thorax and containing displaced abdominal viscera. The malformation is generally discovered by chance in the living as the result of roentgen examination or operation. The condition seldom causes discomfort, and no curative treatment is possible. Case reports of six patients who came under the author's observation are appended.

LANGMANN, New York.

COARCTATION OF THE AORTA. WILFRID SHELDON, Proc. Roy. Soc. Med. **24**: 573 (March) 1931.

A case of coarctation of the aorta was reported in a girl aged 2 years. She was brought to the hospital because she was puny and underweight and had no appetite. Apart from the cardiovascular system no other abnormal physical signs were found. The signs found on examination of the cardiovascular system are given in the report.

WILLIAMSON, New Orleans.

HEREDITARY AND FAMILIAL OXYCEPHALY. WILFRID SHELDON, Proc. Roy. Soc. Med. **24**:574 (March) 1931.

Hereditary and familial oxycephaly was found to be present in a mother and three children. There were other children. The mother stated definitely

that she bore a striking resemblance to her father. The mental development of the mother and her three children had not been impaired by the deformity of the skull.

WILLIAMSON, New Orleans.

COARCTATION OF THE AORTA. LEONARD FINDLAY, Proc. Roy. Soc. Med. **24**: 849 (May) 1931.

A case of coarctation of the aorta was reported in a boy aged 1½ years.

WILLIAMSON, New Orleans.

THE DIFFERENT FORMS OF TORTICOLLIS IN CHILDHOOD. AUGUST REUSS, Kinderärztl. Praxis **2**:145 (April) 1931.

It was formerly thought that the shortening of the sternocleidomastoid muscle in congenital torticollis was due to injury of this muscle at birth, but the latest knowledge makes it probable that this muscle is shortened during fetal life and that the shortening makes it more liable to injury through the passage of the birth canal. The probable cause of the fetal change in the sternocleidomastoid is an abnormal intra-uterine trauma which leads to an ischemic contracture of the muscle. In a few cases an endogenous, hereditary cause must be assumed, especially when there are changes in the cervical vertebrae or when cervical ribs or congenital scoliosis are present.

A spontaneous cure of congenital torticollis takes place only in the purely traumatic forms. In torticollis due to anatomic causes early operation is indicated to prevent secondary changes in the vertebrae. In the severest cases operation is advisable in the first weeks of life; in the milder types it may be deferred until after the sixth month. Instead of the earlier subcutaneous tenotomy, the operation of choice is open myotomy which gives brilliant results.

Acquired forms of torticollis may be due to trauma, rickets, spondylitis and cervical adenitis. Spastic forms and torticollis rheumaticus are also described.

HUENEKENS, Minneapolis.

HORMONAL THERAPY IN PREMATURE BABIES. E. EDELSTEIN, Ztschr. f. Kinderh. **51**:646, 1931.

No influence could be found on the growth of premature babies who were given injections of blood from pregnant women every two days for six months.

EMERSON, Boston.

Acute Infections

PRIMARY TRACHEOBRONCHIAL DIPHTHERIA. V. K. HART and C. N. PEELER, Arch. Otolaryng. **13**:714 (May) 1931.

Respiratory obstruction without laryngeal symptoms is uncommon enough that diphtheria of the tracheobronchial tree must be considered. It has been demonstrated that diphtheria may be primary here and also be limited to the trachea and bronchi. References to work done in this field are given. Symptoms of this condition are: (1) an obstructive type of respiration, with the classic signs, such as epigastric "dipping," retraction of the intercostal spaces and tracheal tug; (2) cyanosis; (3) restlessness; (4) absence of aphonia, viz., a clear voice; (5) emphysema and consequent tympany; (6) toxemia with myocardial involvement, and (7) an expiratory type of dyspnea like that of asthma. An interesting case report is given. Low tracheotomy is recommended in these cases, with repeated aspiration by means of a small catheter inserted through the tracheal cannula.

BARNETT, Chicago.

THE PRESENT STATUS OF PLAUT-VINCENT'S INFECTION. VOSS HARRELL, Arch. Otolaryng. **14**:1 (July) 1931.

Plaut-Vincent's infection is caused by a symbiosis of a fusiform bacillus and a spirochete. Contributing causes are dietary deficiencies, overindulgence in alcohol and tobacco, trauma to the gums and other less common factors. Persons of all ages are susceptible, though the disease is more common between the ages of 20 and 40. It is widespread geographically. The symptoms are sore gums or tonsils, a foul breath and putrid taste, and few or no constitutional manifestations. A grayish-brown membrane over an ulcerated base is seen, the base being tender and hemorrhagic. Some edema and hyperemia of the involved and adjacent structures are present. The gums, tonsils, pharynx, nasal cavities, palate, ear canal, middle ear, wounds and genitalia are affected.

The condition differs from diphtheria in that the exudate is more localized, the infection usually is unilateral, the gums are often affected with the tonsils, the constitutional symptoms are much fewer or absent, and the smears and cultures show the fusiform bacillus and spirochete instead of the diphtheria bacillus. The incubation period is unknown, but probably is less than three weeks. There is an invariable relationship between the fusiform bacillus and the wide-coiled spirochete. The latter is motile. Evidence seems to show that the spirochete is a highly differentiated form of the fusiform bacillus. The organisms are anaerobic and grow best in an acid medium. The spirochetes precede the bacilli in tissue invasion, though the odor is thought to be due to the action of the bacilli.

Treatment varies, but anything that will destroy either the bacillus or the spirochete is efficient, since they are interdependent. The spirocheticides, potassium arsenite, the arsphenamine group and the salts of bismuth are good. Irrigating solutions of potassium permanganate and potassium chlorate and local applications of sodium perborate and hydrogen dioxide, used hot, are of value. The aniline dye group have a more prolonged antiseptic action. The best treatment seems to be a 1.5 per cent aqueous solution of bismuth and sodium tartrate given intramuscularly and the glycerinated solution of the same strength for topical application.

BARNETT, Chicago.

POLIOMYELITIS INCIDENCE LOWER. Health News (New York State Dept. of Health) **8**:197 (Oct. 26) 1931.

The incidence of acute poliomyelitis has shown a marked reduction since Sept. 19, 1931. This report gives the figures for the 1916, 1930 and 1931 epidemics of the disease both for New York City and "upstate" New York.

Cases of Acute Poliomyelitis Reported

	New York City			Upstate		
	1916	1930	1931	1916	1930	1931
First six months	331	15	34	60	29	31
July	3,443	4	620	611	41	47
August	3,927	15	2,114	1,846	165	524
Sept. 1-19	760	5	738	882	165	537
Sept. 20-26	140	5	177	216	61	150
Oct. 27-Oct. 3	135	5	139	204	47	135
Oct. 4-10	103	10	88	138	40	136
Oct. 11-17	50	4	59	119	46	101
Total	8,889	63	3,969	4,076	594	1,661

Over 1,100 persons in the state responded to the appeal for donors of human immune serum during the 1931 epidemic.

AIKMAN, Rochester, N. Y.

MENINGOCOCCIC PURULENT PERICARDITIS COMPLICATING EPIDEMIC CEREBROSPINAL MENINGITIS. ISADORE M. TRACE and CHARLES BERKOVITZ, J. A. M. A. **97**:246 (July 25) 1931.

In a boy aged 13, epidemic meningococcus meningitis complicated by purulent meningococcic pericarditis developed. Aspiration and intrapericardial injections of antimeningococcus serum resulted in complete recovery.

BONAR, Salt Lake City.

PERTUSSIS. W. AMBROSE MCGEE, J. A. M. A. **97**:922 (Sept. 26) 1931.

In a series of 231 cases of pertussis a positive diagnosis was made in 77 cases by signs and symptoms and examinations of the blood, and in 20 cases by signs and symptoms together with isolation of the organism by the cough plate method. The average white cell count was 18,014, while the lymphocyte percentage averaged 62.9. The Schilling differential count gave no consistent data, but it was noted that when there was a relatively high shift to the left and a low nuclear index with a high lymphocyte percentage the results were less formidable. Therapeutic remedies such as vaccines, ephedrine hydrochloride, cough sedatives and ether (rectally) were studied. The outstanding results were obtained when ether was administered rectally.

BONAR, Salt Lake City.

ACUTE SUPPURATIVE PAROTITIS WITH SPONTANEOUS RUPTURE INTO THE EXTERNAL AUDITORY CANAL OCCURRING AS A COMPLICATION OF MUMPS. GEORGE B. BADER, J. A. M. A. **97**:929 (Sept. 26) 1931.

The case occurred in a 3 year old child.

BONAR, Salt Lake City.

THE DIRECT SKIN TEST IN ALLERGY. F. S. SMYTH and K. BAIN, J. Allergy **2**:316 (July) 1931.

"The skin of younger children and infants gives a greater response to trauma than does that of older individuals. This may be due to the liberation of a toxic substance in the skin cells." The intracutaneous test produces a trauma and thus frequently a nonspecific reaction in infants. It may therefore be too delicate for use in infants. Specific skin reactions dependent on the presence of an antibody (reagin of Coca) are rare in infants under 4 months of age, regardless of sensitivity or contact with allergen. With increasing age, the antibody likewise increases, apparently following a general immunologic law. Skin tests may become negative following these conditions: severe allergic reactions, graded therapy, freedom from contact and the administration of epinephrine. Skin reactions may also fail because of faulty preparation of the test substances (allergens) or because of an inability of the subject to form skin test antibody even though he is clinically sensitive.

HOYER, Cincinnati.

THE TOXIN-ANTITOXIN UNION. A. V. STOESSER, J. Infect. Dis. **48**:255 (March) 1931.

The first part of this paper is a concise review of the subject of the union of toxin and antitoxin. The second part consists of experiments tending to illustrate the theory that the union of toxin and antitoxin (antigen and antibody), with neutralization of the former by the latter, is a colloidal absorption phenomenon, which, if once fixed, cannot be dissociated by simple dilutions. Although toxin-antitoxin combinations behave as colloids, this brand of chemistry does not explain the specificity of neutralization, nor is there anything in the present knowledge of colloidal phenomena that does.

TOOMEY, Cleveland.

A Study of Epidemic Meningitis in Missouri: Epidemiological and Administrative Considerations. Ross L. Laybourn, South. M. J. **24**: 678 (Aug.) 1931.

The author believes that the aggressiveness of the strain of the meningococcus as an invader, the number of organisms involved in an infection and the general resistance of the host are of equal importance in the transmission of epidemic meningitis. With strains of the meningococcus that are not aggressive invaders, cases and temporary contact carriers are of secondary importance in the transmission of epidemic meningitis, since contact with such persons rarely results in sufficiently heavy infections to produce the disease. The chronic carrier is not making a successful effort to rid himself of the meningococcus and is the chief source of sporadic cases of epidemic meningitis, since he is intermittently capable of transmitting heavy infections to contacts who might be able to resist the attacks of small numbers of meningococci of slight aggressiveness, but who will succumb to heavier doses of the same organism.

Cases of epidemic meningitis should be isolated, and attendants should wear masks and observe the other precautions commonly employed in cases of disease in which the portal of entry is through the upper respiratory tract. Close contacts should be segregated for an arbitrary length of time. Special attention should be given to ventilation, humidity and freedom from dust in the quarters in which contacts are held.

Schlutz, Chicago.

Diphtheria Immunization in Private Practice. W. W. Anderson, South. M. J. **24**:690 (Aug.) 1931.

The author reports on 500 consecutive cases of diphtheria in children in private practice; 35.6 per cent of the children had been immunized. The occurrence of diphtheria in this series was 0.8 per cent in those who had not been immunized. In 27 of 28 cases, the Schick test was negative after the injection of toxoid. The twenty-eighth patient received both toxoid and toxin-antitoxin. The reactions following toxoid are a little greater than those following toxin-antitoxin. So far, no child has had diphtheria after proper immunization and a subsequent Schick test. For immunization, the author prefers toxoid to toxin-antitoxin.

Schlutz, Chicago.

The Successful Treatment of Purulent Pulmonary Lesions with Intravenous Injections of Alcohol. A. Landau, M. Fejgin and J. Bauer, Presse méd. **39**:523 (April 11) 1931.

The injection of 33 per cent alcohol intravenously in doses of about 25 cc. in acute pulmonary lesions with suppuration shows almost immediate benefits. The alcohol, introduced directly into the venous blood stream, is seized on by the reticulo-endothelial cells of the lungs and exerts a direct bactericidal action. In case a massive dose is given, too much for the lungs to absorb, damage may be done to the liver, as evidenced by a case of jaundice that developed in one patient so treated. To guard against accidents, the administration of insulin when the alcohol is given is advised. Injections are given daily until the condition of the patient indicates that no more is necessary. Improvement is almost immediate, with a drop in temperature, a decrease in the amount of sputum and the clearing up of the pulmonary signs. In two cases reported, the total number of injections was nine each.

Bieker, St. Petersburg, Fla.

Necrosis of the Tonsil Following Diphtheria. Hermann Zischinsky, Jahrb. f. Kinderh. **132**:15 (June) 1931.

In three cases beginning as typical pharyngeal diphtheria, there occurred sudden and rapid necrotic destruction of one or both tonsils. All the patients recovered. No spirillae or fusiform bacilli were found.

Clausen, Rochester, N. Y.

EMPHYSEMA OF THE SKIN IN MEASLES. LIESE GOEBEL, Monatschr. f. Kinderh. **51**:106 (Oct.) 1931.

A 6 year old child suffering from measles developed an emphysema involving the anterior portion of the chest as well as the upper part of the arms. Under treatment with phenobarbital sodium and plenty of oxygen, he made a complete recovery. Cases of this sort have been reported. As a rule the prognosis is good, or at any rate the prognosis is that of the accompanying measles. The occurrence of the complication cannot be attributed to any known factors occurring in measles. It is possible that there is some special toxic effect on the lung tissue in certain cases, permitting an easy rupture. Treatment by incision of the skin to release the air is not necessary. Narcotics, oxygen and sufficient food are the essentials.

GERSTLEY, Chicago.

THE NATURE OF THE EXANTHEM IN SCARLET FEVER AND THE MECHANISM OF THE EXTINCTION PHENOMENON. F. BORMANN and A. WOLFF-EISNER, Ztschr. f. Kinderh. **51**:550, 1931.

The symptoms of scarlet fever are too general to point strongly to anaphylaxis, which as a theory helps in no way but rather brings in unnecessary difficulties. It would seem from all the evidence that the exanthem is caused by the ectotoxin of the scarlet fever streptococci. On the other hand, the extinction factor of the serum with its therapeutic action is identical, apparently, with the antitoxin. The hypothesis of fixation, which fits the problem best, traces the exanthem to the anchoring of the toxin in the skin, its extinction to neutralization by the antitoxin. The possibility of causing a localized immunity in the skin to Dick toxin and to the scarlet fever exanthem, together with the fact that the skin attains its freedom from exanthem, and its power to fix Dick toxin, before the appearance of antitoxin in the blood, offers certain objections to the fixation theory, which are of little consequence if one looks at the toxin-fixing agent of the skin as the mother substance of antitoxin. The healing of the organism from the initial toxicoses may begin in the skin, which, accordingly, may be the place where antitoxin is produced. The maturing of the secreting cell complexes of the skin, lying dormant up to this time, under the influence of the toxemia in addition to the precipitate production of antitoxin, produces a hyperemia of the skin, the exanthem (secretion hypothesis). Scarlet fever has this feature in common with many other exanthems, that its hyperemia is chiefly the result of the action of toxin and congestion; it is thus a nonspecific expression of a specific process in the skin. The extinction phenomenon is due to the fading of the hyperemia in the places where the action of toxin is blocked by the application of antitoxin from local depots. These results refer only to the antitoxin fraction of scarlet fever immunity and in no way to the antibacterial fraction which appears later.

EMERSON, Boston.

THE EXTINCTION PHENOMENON IN SCARLET FEVER. F. v. BORMANN and A. WOLFF-EISNER, Ztschr. f. Kinderh. **51**:560, 1931.

The extinction phenomenon of scarlet fever is clinically a return of the skin areas concerned to normal, the healing of the exanthem, and is in no way a spastic, anemic reaction. Only a fresh and typical exanthem in which as yet no irreversible skin changes exist will show the extinction phenomenon without fail. Atypical rashes and rashes over five days old with their deeper lying skin changes can be extinguished with a small degree of regularity. A serum with a greater content of the extinguishing factor is necessary in the cases of severe intoxication. Only the organism immunized against the scarlet fever streptococcus or its toxin will produce the extinction phenomenon. The biologic type of donor, provided he can be immunized against the scarlet fever streptococcus, is of no importance. Normal serums and those effective against other etiologic agents are not capable

of producing the extinction phenomenon. Böttner's calcium phenomenon is not detrimental to the specificity of the real extinction phenomenon. Only a scarlet fever exanthem can be extinguished by scarlet fever serum; a positive extinction test completely establishes the diagnosis of scarlet fever.

EMERSON, Boston.

PRECIPITATION OF ERYTHROCYTES AS A MEANS OF EARLY DIAGNOSIS IN PERTUSSIS. H. HELMCHEN, Ztschr. f. Kinderh. **51**:643, 1931.

The speed of precipitation of erythrocytes is of practical help in the early diagnosis of pertussis. The rate is slowed when the disease is without complications.

EMERSON, Boston.

Chronic Infections

DESENSITIZATION IN TUBERCULOUS GUINEA-PIGS AS MEASURED BY THE SYSTEMIC TEST. JOHN WEINZIRL and J. DURWARD THAYER, Tubercle **12**: 488 (Aug.) 1931.

Assuming that tuberculosis is primarily a case of sensitization, Weinzirl and Thayer undertook to determine the possibility of desensitizing tuberculous animals in such a manner as to minimize or obliterate the tuberculin reaction. Tuberculin in large doses causes death by severe allergic reaction. Small doses, properly spaced, partially desensitize and allow immunity to develop. The chief factor in the success of the rest cure is the prevention of severe allergic reactions caused by the pouring into the circulation of large doses of tuberculoproteins or tuberculin as a result of exercise. When the body is at rest, these substances are produced in minimal amounts and desensitization rather than allergy is favored. The authors have discarded the skin test as a measure of immunity in tuberculous animals as being too delicate. Instead, the systemic reaction to old tuberculin, manifest by limpness of the muscles, inactivity, anorexia and general prostration, was used to indicate the effects of the antigens. The results of the experimental work indicated, by the systemic test, that considerable desensitization was secured in tuberculous guinea-pigs treated with certain antigens. Desensitization protected the animals, to a considerable extent, against the administration of 25 mg. doses of old tuberculin. Heat-killed tubercle bacilli, iodine-killed bacilli and old tuberculin were found to be unsuitable antigens. Ether killed and treated antigens of both virulent and nonvirulent tubercle bacilli and Mycobacterium smegmatis caused desensitization to about the same degree in suitable doses. Tuberculoproteins have promising possibilities. A dose of 1.0 mg. of bacillary antigen generally gave greater desensitization than smaller doses; larger doses tended to kill the animals. The systemic test as used was found unsatisfactory on account of the toxic properties of old tuberculin. Theoretically, the value of the test was not altered; only the reagent was found deficient. It is hoped that purified tuberculin will prove more satisfactory.

SMITH, Ogden, Utah.

PULMONARY TUBERCULOSIS OF BRONCHOPNEUMONIC FORM, THEN ULCERATIVE, IN AN INFANT ONE MONTH OLD. G. PETROVITCH and L. YOVANOVITCH, Bull. Soc. de pédiat. de Paris **29**:101 (Feb.) 1931.

A boy, 1 month old, began to cough, ran a fever and failed to gain weight as he had done consistently during his first month of life. He showed progressively more marked physical changes in the chest, and roentgenograms revealed shadows of increased density in both lungs which became gradually more marked. The Pirquet test was negative at 14 days of age, but became positive when the patient was 28 days old. The mother had advanced pulmonary tuberculosis. The infant was given B C G by injection and some by mouth, beginning on the nineteenth day after birth. This probably had nothing to do with the course of the disease in

this infant. He died when he was a few days less than 2 months old. At autopsy all the organs were studded with tubercles, but there was no involvement of the meninges or brain. The lower lobe of the left lung contained a cavity and the parietal peritoneum showed some tuberculous nodules.

BENJAMIN, Montreal, Canada.

HEPATIC ASCARIASIS. L. BABONNEIX, Bull. Soc. de pédiat. de Paris **29**:117 (Feb.) 1931.

A girl, 1½ years old, died of bronchopneumonia. There was a history of repeated vomiting and of round worms. Autopsy revealed, in addition to bronchopneumonia, numerous round worms in the liver, some deep in the liver and others as in a cavity just under the capsule at the surface of the liver. Some of the latter were free on the surface of the organ; these must have emigrated from the liver post mortem, as there was no evidence of any peritoneal reaction. There was never any jaundice present during the life of the child, and the liver was not tender on palpation. As in all such cases reported, the liver contained multiple abscesses filled with worms which had doubtless come from the intestine. The intestine was full of round worms.

BENJAMIN, Montreal, Canada.

GOLD THERAPY IN TUBERCULOUS ADENOPATHIES. R. HUGUENIN, M. LIBERSON and Y. DUPONT, Presse méd. **39**:833 (June 6) 1931.

Nine cases of tuberculous adenitis are reported in patients treated with intravenous injections of a solution of hyposulphite of gold and sodium. The dosage must be rather large in comparison with that given in pulmonary tuberculosis, and the total amount of the drug given must be at least 6 Gm. in weekly doses. All the cases reported responded, the degree of improvement depending to a large extent on the regularity with which the patient returned for treatment. The authors feel that this therapy in tuberculous adenitis has great promise.

BIEKER, St. Petersburg, Fla.

TREATMENT OF OSTEO-ARTICULAR TUBERCULOSIS WITH GOLD AND POTASSIUM CYANIDE. FRIEDLAND, Presse méd. **39**:884 (June 13) 1931.

Friedland has for several years used local injections of gold and potassium cyanide in the treatment for osseous and articular tuberculosis. In following fifty cases for two years, he reports success in 84 per cent. The action of the drug is, he believes, directly on the organism. The dosage is from 0.003 Gm. in infants to 0.02 Gm. in adults, in a 1 : 1,000 solution, with the addition of procaine hydrochloride in adults. For children Friedland uses an ether anesthetic. An Esmarch bandage is applied and left in place for fifteen or twenty minutes, in order to obtain as prolonged a local effect as possible. Often one dose is sufficient. If necessary, a second dose may be given in two or three weeks, and in rare instances a third. The usual orthopedic measures must not be neglected.

BIEKER, St. Petersburg, Fla.

KALA-AZAR IN FRANCE. PAUL GIRARD, Presse méd. **39**:1213 (Aug. 15) 1931.

Kala-azar is a tropical disease caused by Leishmania donovani and characterized by irregular fever, marked enlargement of the spleen and sometimes of the liver, leukopenia, with from 80 to 100 per cent mononucleosis, and occasional enlargement of the lymph nodes. The disease was not found in France before the World War, but a number of cases have been reported since, and the year 1930 marked a recrudescence of the disease.

In India, adults are more frequently affected, but most of the victims in France have been children 1 or 2 years of age. The difference seems to be due to climatic and general hygienic conditions. The epidemiology is not quite clear; dogs, ticks,

lice, bedbugs and leeches have been implicated. Children reared in homes where there are gardens or in rural districts are affected, rather than children in cities.

The diagnosis is not difficult, but splenic puncture is necessary to find the organism. Treatment is prolonged and difficult, and consists of the administration of salts of antimony, with ultraviolet rays as a valuable adjuvant.

BIEKER, St. Petersburg, Fla.

DIAGNOSIS OF CONGENITAL OSSEOUS SYPHILIS IN EARLY INFANCY. M. PEHU and A. POLICARD, Presse méd. **39**:1245 (Aug. 22) 1931.

The spirochete invades the skeletal system about the fifth month of fetal life. Only the bones that ossify in cartilage are attacked before birth; those which have their center of ossification in membrane are attacked later. There is a remarkable symmetry of the lesions, and a majority of the bones show invasion, since there is little to hinder the progress of the infection. There is a decided difference between syphilis of early infancy and that of a later period when localization of the spirochetes has taken place. At this later time the lesions are neither generalized nor symmetrical.

The bone lesions of congenital syphilis may be classed as follows: 1. Osteochondritis. This is a lesion of intra-uterine life, disappearing about the third month after birth. Only bones ossifying in cartilage are attacked. 2. Ossifying periostitis. This usually succeeds osteochondritis, but may accompany it. This lesion is of later occurrence and is found, as a rule, after birth. It may attack bones ossifying in membrane. On roentgen examination the bones show concentric lamellae as very regular black lines. 3. Osseous rarefactions. These are seen, on roentgen examination, at the metaphyses or diaphyses of bones of the extremities. They are irregular, with no borders, and vary from the size of a pinhead to that of a bean. The bone may have a "worm-eaten" appearance. These lesions are actual gummas. 4. Exuberant osseous production. This is an actual hyperplasia, usually with cauliflower-like formations of the bones of the extremities. It is a rare lesion. 5. Transverse bands. These are rather rare, and have the appearance of ribbons, seen at the diaphyses. They represent the remains of an osteochondritic process that has survived intra-uterine life.

From the histophysiologic point of view, osseous syphilis is characterized by an exaggeration of osseous absorption. Each of these forms has its characteristic roentgenologic appearance, not easily confused. The only differential problems concern rickets and scurvy, but these conditions, too, have a characteristic picture. During the first year, roentgen observations are an important part of the diagnosis of congenital syphilis. After the first year, the picture is not so characteristic.

The symptoms of osseous syphilis vary. There may be no pain, even with marked lesions, or the pain may be intense, either spontaneous or induced. There may be localized muscular contractions, and the muscles may be in a state of hypertony.

BIEKER, St. Petersburg, Fla.

CLINICAL COMMENT ON THE DEVELOPMENT AND COURSE OF TUBERCULOSIS IN THE EARLY MONTHS OF LIFE. E. RAUTENSTEIN, Jahrb. f. Kinderh. **132**:75 (June) 1931.

The author observed in 12 of 213 children below 1 year of age a positive tuberculin reaction. He describes in detail 7 cases with clinical signs in children under 3 months of age, and stresses the value of repeated roentgen examinations.

CLAUSEN, Rochester, N. Y.

THE SOCIAL PREVENTION OF TUBERCULOSIS AND THE CHILD. A. GOETZL, Wien. klin. Wchnschr. **44**:774 (June 12) 1931.

The work of social prevention of tuberculosis in the child begins during the pregnancy of the mother. It is during this time that the necessary information

is secured, and the question of an eventual interruption of the pregnancy is ventilated. The latter problem would be brought nearer its solution if organized cooperation were obtained between the officers working for the prevention of tuberculosis and the person who has to decide on this step in every single case. The determination of the tubercle bacillus in the circulating blood according to Loewenstein and Fischer will perhaps help to make the indication clear. After birth the baby must be kept away from the predisposing milieu. In this the obstetric departments must cooperate with the social prevention of tuberculosis.

On the basis of increasingly frequent tuberculin tests, the prognosis of tuberculosis in nursing infants proved to be more favorable than it had been believed to be. It must be regarded as most unfavorable for infants in the first three months of life, but improves with age, so much so that the babies infected in the last three months of their first year have practically the same chances as babies infected in the second year of life. The question whether the virulence of the human type of the tubercle bacillus plays a rôle with regard to the infection cannot yet be answered. Calmette and his co-workers in their studies of the tuberculous ultravirus outlined new plans of investigation. According to Redecker, "massive" infection resolves itself into "occasional," "insinuating" and "surprise" infection, with or without consecutive superinfection.

Investigation has revealed that, at the present time, infection by the father is more frequent than infection by the mother, which is probably due to the present social conditions. The effect of the infection depends above all on the age of the infected baby. According to Pollak, the approximate age limit up to which the baby overcomes the primary infection without a manifest morbid syndrome is 4 years; according to Bergmann it is 7 years. Manifest syndromes are, however, observed even if the primary infection takes place after the seventh year. Also here, the mode of infection plays an important rôle.

From the fifth year on, the tuberculosis mortality of girls is slightly higher than that of boys, and from the tenth year on, it is markedly higher. This higher mortality of girls may be explained by constitutional factors, but also by social factors, as girls are more exposed to intradomiciliary infection. Before the child is 2 years old, it must by all means be protected against primary infection or at least against frequent superinfections. Everything must be done to strengthen it by sufficient food and inuring exercises. This prophylaxis against exposure is the most important concern in the first two years of life.

A. F. Abt, Chicago.

Treatment with Gold Preparations for Pulmonary Tuberculosis in Childhood. O. Wiese and L. Hindersin, Ztschr. f. Kinderh. **51**:396, 1931.

Treatment with gold compounds is foreign body therapy. In the days when the production of collapse of the lung was not known, it could have been used, but now there is no real indication for it.

Emerson, Boston.

Syphilis and Tuberculosis. Zahradnicky, Časop. lék. česk. **68**:1096 (Aug. 2); 1129 (Aug. 9); 1159 (Aug. 16); 1188 (Aug. 23) 1929.

Direct inoculation with tuberculosis practically never occurs in the chancre stage, but may take place during the secondary or tertiary stage. Indirect tuberculous infection may take place after a decrease in resistance following syphilitic infection or in congenital syphilis. Syphilitic children have a predisposition to rickets and localized tuberculosis. Sargent stated that syphilization is the terrain of choice for tuberculosis; syphilization in the parents predisposes to tuberculosis in the offspring, and the family history reveals syphilis in children with scrofulotuberculosis. Syphilotuberculosis is divided into scrofula engrafted on old or recent syphilis, or syphilis engrafted on a preexisting scrofulotuberculosis. The differential diagnosis of tuberculosis and syphilis is taken up in minute detail. The

preference of tuberculosis for pulmonary tissue and that of syphilis for nervous tissue is discussed. The differential diagnosis of lesions of the bones, joints, glands, skin and mucous membranes is given in detail. A biblography is appended.

STULIK, Chicago.

THE SIGNIFICANCE OF CALCIUM AND LIPASE LEVELS IN THE BLOOD SERUM OF CHILDREN WITH PULMONARY TUBERCULOSIS; THE EFFECT OF CALCIUM AND LIPOID THERAPY. VLADIMIR DVORSKY and MILOS FIEDLER, Časop. lék. česk. **68**:1156 (Aug. 16); 1192 (Aug. 23) 1929.

In a review of the literature on calcium studies the authors cite a greater output of calcium in the urine, a more rapid tooth decay and other factors as tending to prove the excessive loss of calcium in tuberculosis. A decrease of both ionized calcium and calcium proteinate and the calcium and potassium antagonism is not universally reported. Beneficial calcium therapy must take into consideration the lowered alkaline reserve of the body during tuberculosis. The lipase titer was found to be lower in rapidly progressing tuberculosis and in cases of pleurisy with effusion than in cases with a good prognosis. The antemortem titer is usually low. There seems to be some interrelation between calcium, lipoids and lipase. The serum of fifteen normal persons revealed from 9.5 to 11 mg. of calcium per hundred cubic centimeters and from 18 to 22 mg. of potassium. In seventy-five tuberculous children the calcium titer was lowest in those with severe infection and a poor prognosis. The injection of calcium chloride intravenously and of calcium gluconate intramuscularly revealed a marked temporary increase in calcium in sick and not in normal persons, the reaction being slower and more persistent in the latter. The greatest increase was found in those with the lowest titer originally. The calcium level remained higher when liver lecithin was given. The lipolytic index was decreased in the presence of fibrocaseous tuberculosis and was directly proportional to the prognosis. The injection of gamelan (lipoid) had no effect on the lipase index, but liver lecithin increased the lipase titer appreciably.

STULIK, Chicago.

Internal Diseases

TREATMENT OF TAPEWORM THROUGH DUODENAL TUBE. HERBERT GUNN, Am. J. Trop. Med. **11**:273 (July) 1931.

The author gives a brief review of the literature on the treatment for tapeworm by injection through a duodenal tube, and outlines his method which consists in placing the patient on a liquid diet for a day and a half prior to treatment and in thoroughly emptying the bowels the day before the vermifuge is given. The next day a Rehfuss tube is passed into the duodenum, and an emulsion containing 2 drachms (7.7 Gm.) of oleoresin of aspidium and 1 ounce (28.3 Gm.) of magnesium sulphate is injected in two doses, one-half hour apart. The emulsion should be warmed and injected slowly. One-half hour after the last dose of vermifuge, another one-half ounce (14.1 Gm.) of magnesium sulphate is injected through the tube, and following this, at one-half hour intervals, a syringe full or more of water is injected. If purgation has not begun from two to three hours after the last dose of vermifuge, an enema is given. In case only part of the worm protrudes from the anus, an enema should be given immediately to wash the worm out. The tube should always be left in place until purging begins, if possible. The author has cured twelve of fourteen patients treated by this method.

BURPEE, Augusta, Ga.

ASCENDING URINARY INFECTION: EXPERIMENTAL STUDY. WILLIAM J. CARSON, Arch. Surg. **23**:74 (July) 1931.

The author attempted, with experiments in rabbits, to demonstrate that one of the routes by which infection may travel in reaching the ureter and kidney from the bladder is by extension of the infection by way of the lymphatics. Broth cultures of Staphylococcus aureus and Bacillus coli were used. In three different types of experiments the author was able to demonstrate that infection produced experimentally in the lower end of the ureter or wall of the bladder passes through the perivascular lymphatics to the kidneys. In one experiment the culture reached the kidney when injected into the wall of the ureter; in the second a similar result was obtained when a portion of the ureter was excised, and in the third experiment the injection of culture was made into the fundus of the bladder and reached the kidney.

KAISER, Rochester, N. Y.

CONGENITAL PYLORIC OBSTRUCTION. ORVILLE BARBOUR, J. A. M. A. **97**:455 (Aug. 15) 1931.

The symptoms of congenital pyloric obstruction are dependent on the degree of spasm and the amount of obstruction, and are thought by some to be due to an imbalance of the vegetative nervous system. The indications for surgical intervention vary. The author has found that a therapeutic roentgen test is the most reliable guide. He has also found roentgenotherapy effective; if more than one treatment is indicated, radium therapy is used. The upper part of the chest is irradiated. The effects are thought to be due to a nonspecific protein reaction that stimulates the sympathetic nervous system and inhibits the activity of the vagus system.

BONAR, Salt Lake City.

THE ANEMIAS OF INFANCY AND EARLY CHILDHOOD. LEONARD G. PARSONS, J. A. M. A. **97**:973 (Oct. 3) 1931.

The author classifies the anemias of infancy as follows: (1) those due to a defect of nutrition, including simple or dietetic anemias and endogenous or constitutional anemias; (2) those due to infection; (3) those due to abnormal hemolysis, and (4) those due to a combination of one or more of the preceding causes. The existence of a nutritional anemia in artificially fed infants has been long known, and is probably due to an iron deficiency in milk. These cases usually respond to treatment. Iron and copper preparations, dried yeast and blood transfusions have been used. The constitutional anemias, of which Parsons thinks the so-called "primary anemia of the new-born" is an early form, are of the chlorotic type. These children do not respond to treatment well. The anemias due to infections comprise chiefly those due to intestinal and urinary infections. As to the anemias due to abnormal hemolysis, the question of the relationship between normal hemolysis at birth and the anemias of infancy is discussed. The author believes that the anemia following icterus gravis comes under the head of anemia from hemolysis, that it differs from nutritional anemia and that there is no connection between jaundice at birth and the nutritional type of anemia. He considers that the pseudoleukemia of von Jaksch is not a disease sui generis, but rather a syndrome that may arise from many different causes.

BONAR, Salt Lake City.

ALLERGIC AND INFECTIOUS CONDITIONS OF UPPER RESPIRATORY TRACT IN CHILDREN. M. B. COHEN and J. A. RUDOLPH, J. A. M. A. **97**:980 (Oct. 3) 1931.

By means of tabulations and photomicrographs differences between allergic and infectious respiratory conditions in children were demonstrated. The history of recurrent attacks with wheezing, a relationship to heredity and slight constitutional symptoms, together with the finding of pale mucous membranes, a thin discharge

with 10 per cent or more eosinophils in the smears and roentgenographic evidence of increased bronchial markings, with relief from the use of ephedrine, serve to diagnose the allergic type of ailment.

BONAR, Salt Lake City.

NEPHROSIS IN CHILDHOOD. S. AMBERG, J. A. M. A. **97**:1048 (Oct. 10) 1931.

The term nephrosis was introduced to designate histologic changes in the kidneys manifested by a primary degenerative process of the tubular epithelium in contradistinction to inflammatory changes in interstitial tissue and glomeruli. It is more common in children than in adults. The changes in the tubules vary from cloudy swelling to necrosis. Glomerular changes vary. The lipoid changes are attributed by some to a general metabolic disturbance. Objections to the name have been made, but until knowledge is further advanced it may be well to adhere to a name designating definite histologic changes of an organ that contributes something definite to the clinical picture. Clinically the most striking feature is edema, not only of the skin and muscles but of various viscera and serous cavities, with effusions characterized by a low protein content. The urine is reduced in amount, is of high specific gravity and often contains large amounts of albumin, usually serum albumin. The chloride content of the urine is low; various kinds of doubly refractile lipoids and frequently a large number of unexplained leukocytes are present. The blood proteins are reduced, with an increase of globulin and fibrinogen; the lipoids are increased; nonprotein nitrogen is not increased, sugar is at the lower limit of normal, and calcium and chlorides are usually low. The arterial blood pressure is low. The sensorium of the children is usually alert, and manifestations of edema of the brain are rarely seen. The mortality is high. Restriction of fluid is desirable, and diuresis is employed by the use of ammonium nitrate followed by injections of salyrgan and the oral administration of urea or magnesium sulphate and large doses of thyroid extract. Parathyroid extract and calcium gluconate have been recommended. The children are kept in bed until all data are obtained, on a so-called basal nephritic diet. From an etiologic standpoint, infections are given a prominent place, especially those of the upper respiratory tract. Nasal sinus infection does not seem to be an important factor.

BONAR, Salt Lake City.

ACUTE GLOMERULAR NEPHRITIS IN CHILDREN. K. D. BLACKFAN and C. F. MCKHANN, J. A. M. A. **97**:1052 (Oct. 10) 1931.

Acute glomerular nephritis is usually preceded by an acute illness commonly associated with the hemolytic streptococcus. In children suffering from this type of nephritis, there may develop a picture characterized by vomiting, headache, visual disturbances, slow cardiac and respiratory rates, coma, convulsions and ultimately death. This syndrome has been called uremia, pseudo-uremia or convulsive uremia. Since the condition is unrelated to the retention of nitrogenous end-products, these terms are misleading. The authors prefer to term the condition the cerebral manifestation of acute glomerular nephritis. The systolic and diastolic blood pressures are increased greatly. Edema, while present, is not as marked as in other forms of nephritis, and one gains the impression that 4 or 5 pounds (1.8 to 2.2 Kg.) of edema fluid is held in part as intracellular water rather than as intercellular fluid; this type of intracellular edema is found in various organs, including the brain. The brains have weighed from 20 to 30 per cent more than normal, the convolutions have been flattened, the brain surface has been firm, and at the base there is found the so-called medullary cone phase, produced by pressure of the medulla into the foramen magnum. These changes explain the cerebral manifestations. Magnesium sulphate given by mouth or rectum usually suffices to control and relieve the cerebral symptoms if administration of the salt is begun with the increase in blood pressure and headache and before coma ensues. Large doses are necessary: from 1 to 2 ounces (28.3 to 56.7 Gm.) of a 50 per cent solution by mouth or rectum, given every four hours. These massive doses

do not cause diarrhea. In comatose patients or in those with convulsive twitchings, oral or rectal administration is not effective. The slow intravenous administration of a 2 per cent solution of the anhydrous salt gives prompt relief from the cerebral symptoms and a rapid fall of blood pressure. Lately the observers have used intramuscular injections of a 25 per cent solution of magnesium sulphate as the method of choice. The usual dosage is 0.2 cc. per kilogram. The mechanism of the action of this salt is not entirely clear.

BONAR, Salt Lake City.

SOURCE AND RÔLE OF URINARY PROTEIN IN NEPHRITIS. W. A. THOMAS, J. A. M. A. **97**:1055 (Oct. 10) 1931.

The clinical picture of nephritis is due chiefly to specialized or generalized tissue damage, with a disturbance in tissue metabolism, and to the mineral balance rather than to a lack of renal function with retention of waste products and water. The kidney, whether normal or diseased, acts selectively on the blood proteins, retaining those normal to the body and excreting those foreign to it. The intravenous injection of a 5 per cent solution of sodium chloride produces nephritis and uremia in dogs. At first the urinary protein in these uremias is tissue protein. Tissue protein split to a toxic stage is then combined with serum protein which is excreted as a foreign protein. Serum protein in the urine in nephritis is a detoxicating mechanism.

BONAR, Salt Lake City.

INCIDENCE AND VARIETY OF HEART DISEASE IN SCHOOL CHILDREN OF SAN FRANCISCO. INA M. RICHTER, J. A. M. A. **97**:1060 (Oct. 10) 1931.

The increasing death rate from heart disease has led to many studies that tend to show that with the exception of syphilitic heart disease little is known about the etiology and prevention of heart disease. From 1.5 to 2 per cent of the population seem to be suffering from heart disease. Two per cent of the total school population of San Francisco have been reported as cardiac suspects. Eight hundred and forty-three of these children were examined, and 319 were found to have organic lesions. Clinical study of these children showed that congenital lesions are not uncommon, but symptoms and physical disability are less common than in cases of rheumatic endocardial and myocardial lesions. Valvulitis characteristic of the rheumatic syndrome is not uncommon in San Francisco, but its manifestations are less dramatic and the inception more insidious. The type of lesions following scarlet fever and diphtheria suggests the myocardial lesions of later life.

BONAR, Salt Lake City.

PREPARATION OF BEEF JUICE IN PREVENTION OF BEEF TAPEWORM INFESTATION IN CHILDREN. I. M. LEVIN and I. PILOT, J. A. M. A. **97**:1074 (Oct. 10) 1931.

Raw meat and incompletely boiled or unfiltered beef juice should not be given to young children. A case of Taenia saginata infestation with toxic symptoms in a 2 year old boy is reported following the use of improperly prepared beef juice. If raw beef is used in the preparation of the juice, filtering through muslin or a handkerchief is an effective method of removing possible cysticerci.

BONAR, Salt Lake City.

BASAL METABOLISM AND BLOOD CALCIUM STUDIES IN ASTHMA AND ALLERGIC ECZEMA. R. A. KERN and IDA TELLER, J. Allergy **2**:488 (Sept.) 1931.

The nasal metabolic rate tended to be subnormal in a group of seventy-five patients with asthma (allergic in fifty-five and infectious in twenty) and in eighteen cases of eczema. The percentage of patients having a lower rate was greater in the eczema group. The authors believe that the lowered rate is due to depressed

thyroid function, which is an effect rather than a cause of the allergic state. The blood calcium in the seventy-five asthmatic patients and in three patients with eczema was within the normal limits of 9 and 11 mg.

HOYER, Cincinnati.

JUVENILE ASTHMA. W. O. COLBURN, Nebraska State M. J. **16**:389 (Oct.) 1931.

Asthma is a recurring dyspnea, more marked in expiration, associated with wheezing. It is an allergic manifestation in approximately 50 per cent of cases, favoring a higher percentage in the early years of life. The child with this allergic predisposition should be watched for sensitizations. By an early discovery of these, much can be done for his future health. The neglect of this condition in early life results in extensive pulmonary trauma, with pathologic changes that are unyielding to any known treatment. It is an established fact that eczema precedes asthma in about 50 per cent of the cases. Nose and throat specialists look for focal infection. Every asthma patient should be subjected to an exhaustive examination, including a carefully taken history, a thorough physical examination of the nose, throat and chest, roentgen examination and a laboratory analysis. Perhaps one of the most important procedures is the skin sensitization test, comprising proteins of all classes, foods, inhalants, bacteria and animal emanations; a consideration of physical agents now known to enter into the etiology is also important. Among foods, wheat, egg, milk, fish, meat, potato and spinach are commonly reacted to; among inhalants, feathers, horse, human, cat, dog and rabbit hair, dust, orris root, etc.; among pollens, timothy and ragweed principally, but also all pollinating trees, grasses and weeds. Most cases in the young child are of bronchial asthma and are either associated with, or simulate, infections of the upper respiratory tract. The numerous and varied forms of relief advocated for the cure of this malady only make it apparent that specificity in treatment is far from attainment. Desensitization can be accomplished by repeated frequent subcutaneous injections of extracts of the offending protein in increasing doses. Early treatment in allied asthmatic conditions will result in the relief of 75 per cent of cases of juvenile asthma. The treatment may be palliative or specific, and may include surgical intervention in some instances.

HAMILTON, Omaha.

METABOLISM STUDIES IN COELIAC DISEASE. OLIVE MACRAE and NOAH MORRIS, Arch. Dis. Childhood **6**:75 (April) 1931.

A metabolic investigation was carried out in celiac disease, showing that the defect is one of fat absorption and is due to changes in the physicochemical constitution of the intestinal contents. Fat determination of the feces with the fat intake shows a low percentage of fat absorption. The administration of acid-sodium phosphate seems to favor absorption of fat as does that of sodium glycocholate.

KELLY, Milwaukee.

TWO CASES OF SUB-ACUTE HEPATIC NECROSIS. HAZEL H. C. GREGORY, Arch. Dis. Childhood **6**:101 (April) 1931.

Two cases of subacute hepatic necrosis are described. A girl aged 8 months and a girl aged 2 years showed marked necrosis of the liver at autopsy. The author stresses the fact that in many previously reported cases the etiology is unknown. In these two cases infection seemed to be the etiologic factor.

KELLY, Milwaukee.

A CASE OF CONGENITAL HYPERTROPHIC PYLORIC STENOSIS. W. F. GAISFORD, Arch. Dis. Childhood **6**:111 (April) 1931.

This is a report of a relapse of pyloric stenosis after operation in an infant. The symptoms recurred after a Fredet-Rammstedt operation, and a second opera-

tion was necessary twenty-six days after the first. At the second operation a thickened area, similar and proximal to the first, was found. This cartilaginous area was incised. The infant had received three blood transfusions during the course of treatment. Two days following the third transfusion a loud harsh bruit was heard over the precordia. This murmur persisted for several weeks and then disappeared.

KELLY, Milwaukee.

MALIGNANT HYPERTENSION IN CHILDHOOD. JOHN CRAIG, Arch. Dis. Childhood **6**:157 (June) 1931.

A case of malignant hypertension is described in a girl, 8 years old. Observations at autopsy are given in detail. The symptoms were headache, convulsions, cerebral amaurosis, unconsciousness and transient hemiplegia with a blood pressure at times as high as 250 systolic. The patient was under observation nearly one year. During this time considerable laboratory work was done, which is reported. Autopsy revealed: (*a*) the typical arteriolar changes of essential hypertension in all the organs examined, except the lungs (in the order of severity, the organs affected were: the kidneys, spleen, suprarenals, bladder, liver and voluntary and heart muscle); (*b*) hypertrophy of the large arteries; (*c*) atheroma of the aorta; (*d*) secondary contraction of the left kidney and arteriolosclerotic ischemic atrophies, degenerations and necroses in both kidneys; (*e*) no nephritic changes, and (*f*) lobar pneumonia.

KELLY, Milwaukee.

ACUTE AND CHRONIC NON-TUBERCULOUS PYURIA IN CHILDREN. A. VICTOR NEALE, Arch. Dis. Childhood **6**:165 (June) 1931.

During a five year period, 117 patients with pyuria were admitted to the Children's Hospital, Birmingham. These were more severe cases, as many patients with mild types of pyuria were treated in the outpatient department. The usual period spent in the hospital was from two to four weeks, most cases clearing up quickly under medical treatment. There is no permanent damage to the kidney in these cases. Nine patients died; 8 of these 9 patients were under 1 year of age. Acute coliform infection may have more serious consequences in the infant. Persistent pyuria is due to (*a*) suppurative pyelonephritis, (*b*) infection associated with a congenital malformation in the urinary tract, (*c*) calculus formation or (*d*) residual infection of the posterior urethra or the base of the bladder. The intravenous use of iopax for urographic examination is of great value in the diagnosis of kidney defects. The treatment that has proved of permanent value and that is curative in chronic pyuria associated with renal or ureteral malformation is excision of the diseased part of the upper renal tract in unilateral cases. In bilateral conditions surgical measures are not possible.

KELLY, Milwaukee.

A CASE OF THROMBOCYTOPENIC PURPURA. A. M. KENNEDY, Lancet **2**:237 (Aug. 1) 1931.

A case of chronic thrombocytopenic purpura is recorded in a girl, aged 18, in whom menorrhagia was a special symptom. Ultraviolet irradiation produced no effect on the blood platelets or on the hemoglobin content of the blood. Splenectomy relieved all the symptoms and cured the disease at once, the blood platelets rising quickly to and persisting at about 200,000 per cubic millimeter; the red cells and hemoglobin content reached normal a little later. Seventeen months after splenectomy the patient was well, the blood platelets were 180,000 and the red cells, white cells and hemoglobin had remained normal.

LANGMANN, New York.

INFANTILE HYPERTROPHIC PYLORIC STENOSIS. CAMERON MACLEOD, Lancet **2**: 526 (Sept. 5) 1931.

In the eighteen cases reported, the first five patients (1919-1924) were treated medically, while the remaining thirteen were treated surgically by Rammstedt's operation. All of the five patients treated medically recovered while among the thirteen treated surgically there were three deaths. In three patients the symptoms began at or soon after birth; in the remaining fifteen the average age of onset was three and a half weeks. All but one of the eighteen patients were males, and all but two were breast-fed. In the patients treated medically, citrated milk and peptonized milk were used. Of the patients treated surgically, chloroform and ether anesthesia was employed in three, and two of these developed pneumonia and died. Since 1928, gas and oxygen anesthesia have been used. The other child who died developed an infection of the abdominal wall and the lower part of the abdominal cavity.

LANGMANN, New York.

X-RAY METHOD OF EXPLORING THE PARENCHYMA OF THE LIVER AND SPLEEN. SILVIJE KADRNKA, Schweiz. med. Wchnschr. **61**:425 (May 2) 1931.

A proprietary colloid preparation containing 25 per cent thorium dioxide and 22 per cent metallic thorium is injected intravenously. It is absorbed by the reticuloendothelial system, rendering it opaque to x-rays. The preparation is diluted at least nine times its own volume with dextrose solution (from 5 to 10 per cent), and is sterilized by heating. The injection is made slowly and at body temperature in the same manner as an injection of ordinary dextrose solution or iopax. The first dose is from 0.1 to 0.15 Gm. per kilogram of body weight. The dose is increased to 0.3 or 0.4 Gm. per kilogram, using from four to six injections over a period varying from six to eight days. The average total dose varies from 0.86 to 1.38 Gm. per kilogram. Rabbits have received ten times the maximum dose per kilogram without apparent harm.

The intensity of the shadow depends on the amount injected and on the function of the liver. Following a dosage of 0.19 Gm. per kilogram the edges of the liver are barely visible. A dose of from 0.8 to 1.0 Gm. gives a medium to intense, granite, mottled shadow. The lobules of the liver are visible, and the blood vessels show by contrast. After at least twenty-four hours, roentgenograms may be taken following a cleansing enema. Usually an anteroposterior position (projection) of the upper part of the abdomen is used. For the spleen, Groedel's position is sometimes advantageous. For roentgenograms of the liver, the author chooses an incidence perpendicular to the plane traversing the liver, which forms with the axis of the body an acute angle of from 60 to 70 degrees, open caudally in the case of the dorsoventral position.

The colloid is slowly eliminated at the rate of approximately 50 per cent in three months. The author considers it safe and even favorable to the reticuloendothelial system. Shock is avoided by the small, spaced doses, and tolerance usually increases progressively. Relative contraindications are: glandular deficiencies, blood dyscrasias and deviations (both local and general) in the sympathetic nervous tone; e. g., asthmatic patients at first may have increased attacks. Severe parenchymal changes in the liver or spleen are probably a contraindication. Indications are: tumors, cysts, abscesses and diverse alterations of the liver and spleen.

The author includes in his paper six reproductions of roentgenograms, illustrating the effect of the preparation used. Each reproduction is discussed.

KREITZ, Ann Arbor, Mich.

RECENT ADVANCES IN THE TREATMENT FOR DIABETES MELLITUS. GEORG R. CONSTAM, Schweiz. med. Wchnschr. **61**:540 (June 6) 1931.

The author discusses the symptomatology of diabetes. He advises a more careful consideration of renal glycosuria, especially the type that accompanies the

acute infectious diseases. He reports several cases in which insulin and special diets were used.

Of greater interest is his discussion of synthalin B. He states that guanidine bodies will reduce blood sugar. Synthalin is decamethylendiguanidine. Synthalin B is dodecamethylendiguanidine. The action of guanidine bodies is not identical with that of insulin; hence synthalin B cannot take the place of insulin completely. Experiments by Zunz and LaBarre have shown that synthalin B may cause a secretion of insulin from the pancreas by stimulating the vagus nerve centrally. They also show that hypoglycemia in animals produced by synthalin B often cannot be controlled with dextrose infusion. Overdosage with synthalin causes liver damage, as manifested by icterus. The author states that he has not observed liver damage following the administration of synthalin B, but he advises caution in the dosage. Since synthalin B acts comparatively slowly, it is contraindicated in impending or actual coma. Constam also states that it is contraindicated in diabetic patients who are markedly below standard weight.

KREITZ, Ann Arbor.

ETIOLOGY OF THE SO-CALLED SPASTIC CONDITIONS OF THE GASTRO-INTESTINAL TRACT (PYLOROSPASM, CARDIOSPASM, HIRSCHSPRUNG'S DISEASE). WALTER LEHMANN, Beitr. z. klin. Chir. **151**:395, 1931.

Congenital pyloric stenosis of infancy is congenital only so far as the function of the pyloric ring is disturbed from birth. Constriction of the pyloric ring is compensated by a hypertrophy of the muscular wall of the canal and not of the ring itself. Varied results from the Rammstedt operation are obtained, because at times only the canal musculature is split and the pyloric ring is left alone. Since its function is disturbed, the pyloric ring must be operated on as well as the canal musculature. The author states that the condition is due not to spasm of the ring but to the insufficient opening. Dilatation and hypertrophy of the esophagus occur as congenital disturbances of the cardia. Cardiospasm in later life is often due to some disturbance occurring in early life. Symptoms occur later because there is marked dilatation. The author believes that cardiospasm is due to a spasm of the ring of the cardia that is functional and not anatomic. This is proved by the successful results obtained with gastro-esophageal anastomoses. The author is not convinced that megacolon is congenital. Just as in pyloric stenosis, there is hypertrophy after birth because of disturbed sphincter function. A complete bibliography is given.

RUBIN, Boston.

TREATMENT FOR HIRSCHSPRUNG'S DISEASE. KURT LAQUA, Beitr. z. klin. Chir. **151**:471, 1931.

The author first discusses the medical treatment in Hirschsprung's disease, and states that it is worth while in weak infants or in preparation for an operation. The diet should be poor in starch and have a low residue. A regular stool should be obtained through satisfactory diet, cathartics and enemas. Breast feeding should be prolonged if possible. It is true that in a mild case the patient can get along for many years on this conservative treatment, but since there is a 60 per cent mortality with this method and a 28 per cent mortality with operation, the author feels that the latter method is more satisfactory, especially since function is well restored.

RUBIN, Boston.

TREATMENT OF PYLOROSPASM OF INFANCY. H. SEIDEL, Beitr. z. klin. Chir. **151**:483, 1931.

The author discusses the dietary and medicinal treatment for pylorospasm with the varying results. The mortality is about 10.2 per cent with this type of treatment. He discusses various operations, such as jejunostomy, pyloric resection, gastro-enterostomy and variations of these procedures. However, he states that

the best results were obtained with the Weber-Rammstedt operation, which showed a mortality of only 4.9 per cent. This is significant because in many cases an operation is performed on infants that have had unsuccessful conservative treatment.

RUBIN, Boston.

FOCAL INFECTIONS. HANS RIETSCHEL and OTHERS, Kinderärztl. Praxis **2**:75 (Feb.); 126 (March); 174 (April) 1931.

Rietschel opens a general discussion of focal infection in childhood, with particular reference to the tonsils, adenoids, teeth and accessory nasal sinuses. The question is discussed by Bieling, Husler, Adrion, Max Meyer, Franz Lust, Koenigsberger, Leichtentritt and Reiche. Rietschel, in his summing up, takes a skeptical attitude toward the removal of foci of infection, especially the enucleation of the tonsils. In acute glomerular nephritis, he contends, there is no tendency to recurrence, even when the focus of infection is not removed, while the prognosis of chronic nephritis and nephrosis is bad no matter what measures are taken. He is equally doubtful as to the value of tonsillectomy in acute articular rheumatism and early endocarditis, even though Leichtentritt is very enthusiastic about his results. Rietschel's final conclusion is that little is known about focal infection and that the therapeutic results of tonsillectomy do not offer any dependable information as to the indications for this operation.

HUENEKENS, Minneapolis.

FREQUENCY, SYMPTOMS AND TREATMENT OF ASCARIASIS. H. NOWAK, Med. Klin. **27**:581 (April 17) 1931.

In investigations among 1,934 children and adults, ascarides were found in 1,404, that is, in 72.5 per cent. This is a higher incidence than that given in former reports. The occurrence is highest between 5 and 15 years. Males show a higher occurrence than females. The highest incidence of the infection is in spring and summer. No symptoms were noted that could be attributed to migration of the embryos through the lungs. Fulleborn's skin reaction is not reliable. For treatment, chenopodium oil was used. No untoward effects were seen. A complete cure was obtained in 75 per cent of the cases.

ZENTAY, St. Louis.

THE INFLUENCE OF PERIPHERAL CIRCULATION ON ALIMENTARY HYPERGLYCEMIA. R. LOEBEL, Wien. Arch. f. inn. Med. **21**:387 (July) 1931.

The author found increased alimentary hyperglycemia in a group of cases in which the mobility of the extremities was distinctly limited (i. e., arthritis, neuralgia, hemiplegia and fracture). Measures that in any way affected circulatory conditions unfavorably (congestion, elevation) caused a still further increase. The injection of sodium nitrate decreased the alimentary hyperglycemia. Neither the fasting blood sugar nor alimentary hyperglycemia is influenced by hot baths or by dry heat. The sugar tolerance may be unfavorably affected by these measures. Cool baths and temperatures have the effect of increasing both the fasting sugar and the alimentary hyperglycemia. The author explains this phenomenon on the basis of a deficiency of the peripheral circulation.

SCHLUTZ, Chicago.

A TERATOMA OF THE OVARY WITH METASTASES RESEMBLING CHORIONEPITHELIOMA AS THE CAUSE OF PREMATURE PUBERTY WITH A POSITIVE PREGNANCY REACTION. H. FASOLD, Ztschr. f. Kinderh. **51**:519, 1931.

A case of premature puberty is described in a girl, 8½ years old, who had been well until two years before, when she began to bleed from the vagina at intervals and grow rapidly in height. On admission she was 20 cm. above the normal height, and looked like a girl who had passed puberty. On rectal examination a tumor the size of a mandarin was found connected with a hard uterus the size of a castaña. There was a cystic tumor at the angle of the right jaw, one near the right lobe of the thyroid, another near the right frontal eminence

and one at the left sternoclavicular joint. A roentgenogram of the lungs showed a shadow in the right upper field, and ossification had been completed in the wrist. Histologic examination of an excised tumor revealed a structure that was like that of a syncytioma malignum. The Aschheim-Zondek reaction for pregnancy was positive. It may be that the tumors caused a flooding of the organism with the hormones of the anterior lobe of the hypophysis, which, according to the present theory, can produce premature sexual maturity.

EMERSON, Boston.

WERLHOF'S DISEASE WITH AN ALLERGIC REACTION TO THE MATERNAL BLOOD OF THE SAME GROUP. H. N. BRINNITZER, Ztschr. f. Kinderh. **51**:566, 1931.

Thrombopenia and anaphylaxis have certain relations to one another. A case of Werlhof's disease is reported which showed definite anaphylactic reactions to the maternal blood of the same group, which disappeared after the injection of serum from a donor. There is a discussion of transfusions of blood of the same group in the transition cases and of repeated transfusions. The marked reaction to maternal blood of the same group, the authors believe, can be traced to the anaphylactic component of Werlhof's disease. Transfusions in such cases must be carried out with especial care.

EMERSON, Boston.

Nervous Diseases

EXPERIMENTAL POLIOMYELITIS: HISTOLOGY OF PERSISTENT LESIONS OF THE CENTRAL NERVOUS SYSTEM. BETTINA WARBURG, Arch. Neurol. & Psychiat. **25**:1191 (June) 1931.

A careful histologic study of poliomyelitis was made to determine the extent and nature of the destructive and repair processes. Fifteen monkeys that had survived from nineteen to three hundred and nine days after the onset of the condition were used. Pathologic changes were found in all cases. Inflammatory areas persisted in the nervous systems of 4 animals that had made a good functional recovery. Regardless of the route of infection, the lumbar cord was most severely damaged in all but 1 case. The thoracic region was not spared to any appreciable extent. The type of lesions found corresponded roughly to the duration of the disease. Diffuse and local infiltrations were found in the spinal ganglions in seven cases. Fewer but definite changes were found in the medulla, pons, midbrain, basal ganglions, cortex and cerebellum in many cases. "It seems likely, probably, that processes may continue to smolder on after the acute symptoms have disappeared, thus suggesting that prolonged rest may be indicated before reconstructive therapy is begun."

BEVERLY, Chicago.

SCHILDER'S DISEASE. GUNNAR K. LAURITZEN and ISAK L. H. LUNDHOLM, Arch. Neurol. & Psychiat. **25**:1233 (June) 1931.

A case of Schilder's disease is reported, and a review of the literature and general comments on the variations of the clinical symptoms and pathologic picture are given. The patient was a 6½ year old boy. In this case an early and rather uncommon symptom was deafness due to inflammation of the temporal lobe. Central blindness, which is often an early finding, did not appear until late in the course of the illness. As is usually the case, an altered sensorium ranging from disorientation and slight apathy to stupor or profound coma toward the end was an outstanding symptom. Foci located in the region under the central convolutions gave rise to tetraplegia. This patient had convulsive seizures early in the course of the disease, which is another uncommon symptom. It is pointed out that cases occur with foci located in the other areas of the brain, i. e., the pons, medulla or basal ganglions, with corresponding symptoms. There are practically no changes in the cranial nerves. Symptoms of increased intracranial pressure are common.

BEVERLY, Chicago.

CEREBRAL BIRTH PALSIES: A CONTRIBUTION TO THEIR PATHOLOGY WITH A REPORT OF A HITHERTO UNDESCRIBED FORM. LEON FREEDOM, Arch. Neurol. & Psychiat. **26**:524 (Sept.) 1931.

There are many diseases that give rise to the clinical picture of infantile palsy. While difficult labor with resulting hemorrhage may be the chief etiologic factor in many cases, it is not the universal or whole cause. Lack of development, inflammatory processes and progressive degenerative disease of various types contribute to the group. The author gives the detailed microscopic observations in a case that had been considered Little's disease (birth injury) with palsy and idiocy. A cerebral degenerative process of unknown etiology was found. A hemorrhage could not have played any part in the picture.

BEVERLY, Chicago.

THE CEREBRAL LESIONS IN PURULENT MENINGITIS. FREDERIC WERTHAM, Arch. Neurol. & Psychiat. **26**:549 (Sept.) 1931.

Histologic observations on the brain substance in twenty-four cases of purulent meningitis are reported. Apart from encephalitic and toxic degenerative changes hitherto described, other extensive lesions occurred. There were marked changes in the cortex and also in the subcortical structures, such as the basal ganglions. Most of the lesions had a circulatory basis. In children, the changes in the deeper structures of the brain were especially pronounced. Toxic factors probably played a minor rôle.

BEVERLY, Chicago.

PHENYLETHYLHYDANTOIN: ITS USE IN CHOREA. S. W. MARICK, Arch. Pediat. **48**:525 (Aug.) 1931.

Over a score of patients with mild and moderately severe chorea were treated with phenylethylhydantoin. A dose of 0.3 Gm. daily was the usual dose, and no bad results occurred. The author recognizes the possible dangers in the use of this drug, but believes such mishaps rare. No rash occurred in one third of the cases reported, yet improvement was noticed in the absence of a rash. The dosages and methods of administration are discussed.

WADDELL, University, Va.

THE MECHANISM OF THE KETOGENIC DIET IN EPILEPSY. EDWARD M. BRIDGE and L. V. IOB, Bull. Johns Hopkins Hosp. **48**:373 (June) 1931.

Evidence is presented showing that neither the ketosis nor the acidosis accompanying the so-called ketogenic treatments for epilepsy can be considered the sole beneficial factor of such regimens. Experiments showed that if the high fat diet has succeeded in removing a surplus of extracellular fluid from the body, improvement in seizures is associated; if the diet has not removed this fluid, it has not affected the course of the disease. Since a simple acidosis and a sodium-free diet also tend to produce similar losses of fluid from the body, fasting may be considered a triple mechanism—a high fat diet, a sodium-free diet and acidosis—for the removal of extracellular fluid, while the ketogenic diet has only two factors: a high fat diet and acidosis. Since no ketogenic diet can be considered a failure until it has failed to maintain the good effects of fasting, it is believed that the institution of the high fat diet should always be preceded by a minimum of five days of complete starvation, only water being allowed. Although the data here presented have been obtained from children with petit mal, there is no apparent reason to suppose that they do not apply to children with major convulsions.

AUTHORS' SUMMARY.

A Case of Progressive Neural Muscular Atrophy. Samuel Joseph Weinberg, Bull. Johns Hopkins Hosp. **49**:61 (Aug.) 1931.

A case of neural muscular atrophy (Charcot, Marie, Tooth) is described in a man aged 20. The condition began at the age of 2 years with areas of cyanosis and sores at various places on the feet and hands. Wasting of the leg muscles was noticed at 10 years, and since that time, atrophy and deformity had made rapid progress. Sores appearing and healing left dense indurated scars on the bony projections of the extremities. No paralyses, tremors, nystagmus or ataxia had been noted. Late in the course of the disease there were extreme degrees of atrophy with contractions and deformity. The cranial nerves were normal, and the musculature of the neck and trunk was of unimpaired strength. There were no fibrillary twitchings over atrophied muscles and no sensory changes. Deep muscle sensibility is unimpaired. Electrical examination showed normal response. A nephew of the patient, aged 2 years and 9 months, was found to be entirely normal except for a condition of the feet. All toes of the left foot and two toes of the right foot were cyanosed, and a number of reddish-blue areas were observed along the margins of the feet. This condition was said to be identical with the early changes in the patient. The differential diagnosis, the literature and what is known of the pathology are discussed.

Lyttle, New York.

Meningococcus Infections Including Meningitis. W. W. Herrick, Bull. New York Acad. Med. **7**:487 (July) 1931.

The meningococcus has been found in almost every organ of the body. It has been associated with endocarditis, septicemia, meningitis, pneumonia, pleurisy, peritonitis, epididymitis, suprarenal necrosis and hemorrhage, encephalitis, suppuration of the paranasal sinuses, tonsillitis and pharyngitis. It is a pyogenic coccus, and in many of its clinical and laboratory manifestations it is analogous to the pneumococcus. It may be divided into several groups or types with varying immunologic properties. In the preparation and administration of the serum it should be remembered that the group may vary in a given epidemic, thus defying classification.

The clinical manifestations of the infection may be divided into three stages: 1. The carrier stage with involvement of one, several or all of the upper air passages, lasting a few days (chronic carriers emit the infection in nasal or sputum discharges, but are themselves immune). The infection may not go beyond this stage (coryza, pharyngitis, sinusitis or tonsillitis). There may be a mild toxemia or no symptoms of importance. 2. The bacteremia stage. Fever and prostration occur; the temperature may vary from subnormal to a very high degree, the average being around 102 F. There may be a chill at the onset of this toxemia. The important feature in this disease is the effect of the toxin on the higher centers. The patient is stupefied, with a blank expression and monosyllabic replies. Attempt at movement is resented, there being a general soreness of all the muscles, in some cases simulating acute polyarthritis. Vasomotor disturbances are manifest in a mottled pallor with patchy suffusion of the face (tache cérébrale). The hemorrhagic rash of the skin is almost pathognomonic. This consists of minute hemorrhages into the skin, varying from pinhead size to several inches in diameter, or in fulminating cases of a diffuse purpura. The rash does not disappear on pressure. Its most common site is around the pelvic girdle and, in more severe cases, over the trunk, conjunctivae, mucosae, extremities or even the face. The rash comes out suddenly. In severe cases these spots become necrotic, suggesting vascular thrombosis. This phenomenon also explains the frequent arthralgias or arthritis encountered as complications of the disease. There is a high polymorphonuclear leukocytosis. The meningococcus may be isolated from the upper air passages, the blood stream, the skin lesions and even the clear spinal fluid. Symptoms of meningeal irritation may be entirely absent in this stage or may occur simultaneously with it. This stage may last from a few hours to

a few days before the development of meningitis. 3. The meningitic stage. The meninges are involved in at least 90 per cent of the meningococcus infections. This stage is ushered in by a bursting headache, vomiting, delirium, a stiff neck and marked irritability. In infants there is failure to nurse, a bulging fontanel, ophthalmoplegia and at times Cheyne-Stokes respiration. Within a few hours the spinal fluid will show from 90 to 100 per cent polymorphonuclears of the white cells present, with fibrin, red blood cells and meningococci. The organism, at first extracellular, may soon be found in the cells. With the administration of serum the spinal fluid begins to clear, but excessive secretion may last for some time afterward.

Cases not yielding to treatment are usually due to encephalitic involvement, a condition insufficiently stressed. The acute increase in the bulk of the brain (engorgement of vessels, edema and perivascular exudate) may give rise to wedging of the brain stem into the foramen magnum. This may be manifest by engorgement of the face and veins of the forehead, agonizing headache, wild delirium and slow pulse rate. It may terminate in sudden death. Another accident of importance is subarachnoid block. The organized exudate in meningitis may close the circuit at any point, causing accumulation of fluid and distention of the ventricles or other subarachnoid spaces, producing hydrocephalus or hydrocephalic meningitis. Among the other serious complications facial nerve paralysis and eighth nerve deafness are not infrequent. In this case the deafness is usually permanent.

The course of the disease is variable, and no definite prognosis should be given as the outcome is not determinable. Relapses are common. When adequate amounts of suitable serum are given within forty-eight hours of the onset, the mortality is about 12 per cent. The mortality tends to rise 10 per cent for each twenty-four hours' delay in treatment. If the response to the serum is not effective promptly, serum from another source should be used in the hope of securing a product containing the proper antibodies. Any complication or accident in the course of the disease should receive careful and prompt attention. Mechanical accidents (block) require immediate relief by drainage (cisternal puncture, ventricular drainage). To ward off recurrences, it may be wise to use meningococcic vaccine during convalescence.

JAHR, Omaha.

RESPIRATORY FAILURE IN POLIOMYELITIS: ITS TREATMENT WITH THE DRINKER RESPIRATOR. E. B. SHAW, H. E. THELANDER and M. A. LIMPER, California & West. Med. **35**:5 (July) 1931.

Fifteen cases are reported of patients suffering from various respiratory paralyses due to poliomyelitis, treated by means of the Drinker respirator. Of the nine patients having intercostal paralyses, all were benefited by the treatment, although three died, one because treatment had to be discontinued, and two because of other complications. One patient had chiefly a paralysis of the diaphragm and seemed to be recovering. Of the five patients having bulbar involvement, all died, but subjective relief was noted in several. The authors conclude that intercostal paralysis is the most favorable type for treatment in the respirator, that the treatment not only is a life-saving measure, but helps increase chest expansion, and in milder forms of paralysis provides rest during convalescence.

DICKEY, San Francisco.

A CASE OF DIABETES INSIPIDUS OCCURRING AS A SEQUEL TO EPIDEMIC ENCEPHALITIS. R. W. WHITEHEAD and W. DARLEY, Endocrinology **15**:286 (July-Aug.) 1931.

A case of diabetes insipidus of more than average severity in a boy of 14 years is presented, which evidently had its origin as a sequel to epidemic encephalitis. On admission to the hospital the patient had marked polyuria and polydipsia, with

the voiding of from 8 to 10 gallons (30.2 to 37.8 liters) of urine per twenty-four hours. After a control period posterior lobe pituitary extract was given with no favorable effect, but the pressor principle of the pituitary body was effective in reducing the water exchange to a much lower level. Later additional therapeutic measures consisted in giving the patient warm water to drink and reducing the carbohydrate and salt intake; these were found to be helpful. An unexplained fact is that the substitution of the oxytocic principle for the pressor principle brought about no increase in fluid intake or volume of urine. A number of cases of diabetes insipidus have been reported as occurring after an attack of encephalitis. Presumably the area of the brain that is injured is the same as the area operative injury of which produces experimental diabetes insipidus, namely, the hypothalamus. The evidence is suggestive that the hypophysis, to which nerve fibers pass from this region, is concerned in the etiology of the condition. In the case reported, results show clearly that the pressor principle had only a temporary antidiuretic effect which tended to disappear in three hours or less. JACOBSEN, Buffalo.

SOME NOTES ON MENINGOCOCCIC MENINGITIS, WITH ESPECIAL REFERENCE TO THE SUGAR CONTENT OF THE CEREBROSPINAL FLUID. J. H. MUSSER and J. H. WATKINS, Internat. Clin. **2**:35 (June) 1931.

The authors present a clinical study of sixty-five cases of meningococcic meningitis. The prognosis is unfavorable in cases with an acute onset of fulminating symptoms. An extensive rash is usually an unfavorable sign. In favorable cases meningococci disappear rapidly from smears. The most positive and definite prognostic sign associated with clinical improvement was a return of the dextrose content from an initial low to a relatively normal level.

MILLER, South Bend, Ind.

SLEEP PRODUCED BY HYPNOTICS STUDIED BY THE ELECTRICAL SKIN RESISTANCE METHOD. CURT P. RICHTER, J. Pharmacol. & Exper. Therap. **42**:471 (Aug.) 1931.

The author has shown previously that the electrical resistance of the skin on the palms of the hands of human adults and infants and monkeys is greatly increased during sleep. He now reports that the skin of the palms and soles of cats reacted similarly to that of human beings, and that cats under the influence of hypnotics (paraldehyde, chloral hydrate and sodium amytal) showed an increase in the electrical resistance of the skin similar to, but greater than, that in natural sleep, the greater degree being due to the deeper narcosis, although with paraldehyde the resistance increased to a high level before deep sleep appeared. Paraldehyde was as effective as the other drugs, but recovery was more prompt, an advantage that is clinically demonstrable.

PILCHER, Cleveland.

NEUROLOGICAL DEFECTS OBSERVED IN THE MEDICAL INSPECTION OF SCHOOL CHILDREN. DAVID M. NATANSON, M. J. & Rec. **134**:19 (July 1) 1931.

In children of school age the commonly observed neurologic defects are: chorea, tics, "nervousness," enuresis, mannerisms, epilepsy, mongolian idiocy, mental defectiveness, retardation sequelae of epidemic encephalitis, and temperamental disturbances. The author discusses these defects and suggests means of prophylaxis, but does not enter into the treatment, as the school physician refers the cases to the proper authorities for care and further observation after his examination.

WILLIAMSON, New Orleans.

NEUROSIS IN CHILDHOOD. I. M. ALLEN, Brit. J. Child. Dis. **28**:177 (July-Sept.) 1931.

Among the factors considered responsible for the development of neurosis in childhood are: (1) physical and mental disturbances, (2) a biochemical disturbance, (3) physical habits, (4) the position of the child in the family and (5) a lack of parental training. Under exciting factors such topics as "the birth of the next child," "illness in early childhood," "failure of social adaptation" and "school discipline" are taken up briefly. The manner in which these neuroses of childhood express themselves are exemplified by fears and apprehensions, sleep disturbances, behavior disturbances and tics. An outline of treatment is given under the headings of (1) prophylactic, (2) symptomatic and (3) psychologic.

LANGMANN, New York.

GANGLIONIC NEUROMA OF THE CORD. W. G. WYLLIE, Proc. Roy. Soc. Med. **24**:1050 (June) 1931.

A boy, aged 8 years, was well until November, 1929, when he suddenly became paralyzed in both legs, following an attack of bronchitis. He was admitted to the hospital in April, 1930, with a lobulated swelling 2½ by 2 inches (5.1 by 6.3 cm.) present on the back in the region of the right fifth and sixth ribs after an attack of mumps. The abdominal reflexes were absent bilaterally below and present above. In May, the extrathoracic portion of the tumor was removed and the fifth and sixth ribs resected for 3 inches (7.6 cm.). Subsequently cutaneous analgesia and anesthesia were complete up to the seventh dorsal, and incontinence of urine and feces occurred on several occasions. In October, rapid improvement began. The intrathoracic part of the tumor was exposed and radium needles were inserted, and removed a week later. Empyema developed and healed uneventfully. On discharge the patient was able to walk with a broad base without assistance. On section the tumor proved to be a ganglionic neuroma.

WILLIAMSON, New Orleans.

JAW-WINKING PHENOMENON, WITH CINEMATOGRAPHIC DEMONSTRATION. LEONARD FINDLAY, Proc. Roy. Soc. Med. **24**:1335 (Aug.) 1931.

Jaw-winking was reported in a healthy boy of 14 months. Ever since his birth the mother had noticed that the left eye turned inward and that the left upper eyelid twitched when the child was feeding. She had also noted that while the child was sleeping the left eye was frequently kept open. On examination it was noticed that when he was sitting up there was definite ptosis of the left upper eyelid, and that during eating rhythmic contractions of the levator palpebrae superioris of the left upper eyelid were striking. A cinema film revealed that the contraction of the eyelid was synchronous with the closure of the jaw.

WILLIAMSON, New Orleans.

JUVENILE GENERAL PARALYSIS AND COMBINED SCLEROSIS OF THE MEDULLA. LARUELLE and HEERNU, J. de neurol. et de psychiat. **31**:106 (Feb.) 1931.

The authors present the case of a girl, aged 17 years, who showed psychic disturbances of general paralysis, which had developed at the age of 14 and were progressive. She showed neurologic evidence of pyramidal tract involvement and normal knee jerks, but a positive Babinski sign on both sides and a suggestion of tabes dorsalis in the loss of achilles jerks. The syphilitic nature of the involvement was substantiated by the presence of Argyll Robertson pupils and by positive serologic tests. The interesting feature of the case is that the authors conclude that it is a symptom complex of hereditary syphilis.

WAGGONER, Ann Arbor, Mich.

INORGANIC PHOSPHORUS IN THE CEREBROSPINAL FLUID. A. IÀNCU and BENETATO, Nourrisson **19**:154 (May) 1931.

The spinal fluids of thirty-four infants suffering from a variety of diseases were studied; twenty-eight were less than 1 year of age, and six, more than 1 year. In the former group, the inorganic phosphorus varied from 1.25 to 2.27 mg. per hundred cubic centimeters, with an average of 1.77 mg. Four of those showing an elevation were suffering from congenital syphilis. Other than this there was no definite relationship between the pathologic condition present and the amount of inorganic phosphorus in the cerebrospinal fluid. Reference is made to articles in the American and German literatures.

McCLELLAND, Cleveland.

THE EPILEPTOID INFANT. G. ROBIN, Progrès méd., Aug. 29, 1931, p. 1527.

Two examples are given of the epileptoid child. These children do not have true epileptic attacks, but as infants are subject to tantrums and emotional outbursts. When they are older, they are cruel, treacherous, emotional and theatrical. They react well to epileptic therapy.

SANFORD, Chicago.

IMITATIVE AND MIMIC ABILITIES OF YOUNGER CHILDREN. H. VON RESTORFF, Ztschr. f. Kinderforsch. **38**:411 (May 7) 1931.

Children between the ages of 5 and 8 years were shown pictures of certain attitudes and bodily expressions. Their spontaneous or induced attempts to imitate these pictures were observed.

REICHLE, Cleveland.

VEGETATIVE NERVOUS SYSTEM IN CHILDREN. J. STYTSCHINSKI, Ztschr. f. Kinderforsch. **38**:452 (May 7) 1931.

The reflex obtained by pressure on the eyeball was the test method used. The author believes that he has demonstrated an increased tone of the parasympathetic system.

REICHLE, Cleveland.

EXAMINATION IN TWO CASES OF DEFICIENCY IN READING ABILITY. MARIE WAWRIK, Ztschr. f. Kinderforsch. **38**:462 (May 7) 1931.

The article presents the details of an examination of two patients deficient in reading ability.

REICHLE, Cleveland.

PERCEPTION OF SPACE OF A CHILD THREE YEARS OF AGE. ERNST LAU, Ztschr. f. Kinderforsch. **38**:516 (May 7) 1931.

The author's child at the age of 3 years showed a well developed perception of space in the horizontal direction, but a poor one for space in the vertical. This was shown by its interpretation of the size of the celestial bodies and their distance from the earth. The perception of space in a child is therefore very similar to that of the human being of antiquity.

REICHLE, Cleveland.

THE DEVELOPMENT OF THE INDIVIDUAL'S ATTITUDE TOWARD THE MODERN COMMERCIAL WORLD. ELIASBERG, Ztschr. f. Kinderforsch. **38**:523 (June 29) 1931.

An attempt is made to trace the development of certain conceptions, such as property, work and social standing, from the primitive ideas of the child.

REICHLE, Cleveland.

VARIATION IN THE CHARACTERISTICS OF HANDWRITING. A. LEGRÜN, Ztschr. f. Kinderforsch. **38**:554 (June 29) 1931.

A schoolgirl was observed for several years, and during this time she showed an extreme variation in the characteristics of her handwriting. Her character and development were those of a psychopath.

REICHLE, Cleveland.

THE RESULTS OF THE TRAINING OF SCHOOL CHILDREN WITH SPEECH DEFECTS. KARL C. ROTHE, Ztschr. f. Kinderforsch. **38**:560 (June 29) 1931.

Statistics are offered to show the results of training in cases of speech defect in school children of Vienna. The author emphasizes the great importance of early training.

REICHLE, Cleveland.

THE TREATMENT FOR LATERAL SIGMATISM. E. REINKE, Ztschr. f. Kinderforsch. **38**:565 (June 29) 1931.

The article deals with the treatment of children for lateral sigmatism.

REICHLE, Cleveland.

THE NATIVE INTELLIGENCE OF TWINS. ERICH STERN, Ztschr. f. Kinderforsch. **38**:581 (June 29) 1931.

A pair of male twins, 6 years old, were studied by the author. He states that they were monozygotic; photographs are published, showing that the two boys were unusually similar, but no attempt was made to study them according to the method of Siemens. The various intelligence and behavior tests demonstrated an unusual degree of similarity, but further examinations of the children and, in particular, examinations by the teacher showed that there were definite and fundamental differences in the character and spiritual attitude of the two children. In other words, Stern has again demonstrated, as Lange, did, that the similarity of twins does not exclude the possibility of their developing different personalities. These differences cannot altogether be ascribed to environmental effects.

REICHLE, Cleveland.

SOCIAL STANDING OF THE CHILD AND ITS INFLUENCE ON INTELLIGENCE AND ABILITY IN SCHOOL. A. ARGELANDER, Ztschr. f. Kinderforsch. **38**:589 (June 29) 1931.

The statistical material was divided into two groups: students in routine classes and those in special classes for children who had fallen behind in their schoolwork. The author was not able to establish any relation between the social status of the students in the first group and their native intelligence or class marks. Even among the students in the second class this relation was only slight. It is therefore possible that among students of the second group there were several subgroups, and that some of these students had a normal intelligence which had been affected by their social standing. The other subgroup was probably composed of children whose intelligence was primarily low.

REICHLE, Cleveland.

MONGOLISM IN TWINS. H. OREL, Ztschr. f. Kinderh. **51**:31 (May) 1931.

Orel has reported two pairs of twins in which mongolian idiocy appeared, and has seen two more, one of which is presented here. The babies were of the same sex; one was a mongolian idiot, and although the fetal membranes were not seen, it is probable from the difference in blood groups that the twins were biovular. In the literature there are fifty-one cases in which one or both babies were mongolian idiots, eighteen twins of unlike sex and twenty-nine of like sex. In none of the eighteen was there more than one mongolian idiot. If the cause had been intra-uterine, both babies would have been affected. Under this assumption, mon-

golian idiocy should be infrequent among the different children of the same family. In the entire literature there are only twenty-one families in which there was more than one mongolian idiot. Since in no case when the sexes were unlike was there more than one mongolian idiot, it can be assumed that when there is one the twins are of the biovular type. Among twins of this type there is about an equal number of babies of like sex and of unlike sex. Accordingly, one should expect about eighteen pairs of this series to be of like sex, and in fact there were twenty-two. In the seven remaining pairs, both babies were mongolian idiots and must have been of the uniovular type, in which complete or almost complete resemblance is characteristic. The number of boys and girls was about equal. According to Husler, a distant relationship between the parents is frequent. Orel has seen 180 mongolian idiots, and is uncertain whether the defect can be inherited or not. Considering the laws against the marriage of related persons and the registry for the number of dispensations granted, and comparing this with the total number of marriages over a number of years among the inhabitants of Vienna and of the surrounding country, the percentage of marriages of related persons who later became the parents of a mongolian idiot, is about 0.5 per cent, a number so small as to make it improbable that mongolian idiocy is inherited. One is forced to assume that some unknown injury of the germ cells or the impregnated egg leads to the condition.

EMERSON, Boston.

CONVALESCENT SERUM IN ACUTE POLIOMYELITIS. A. LICHTENSTEIN, Ztschr. f. Kinderh. **51**:39 (May) 1931.

In a study of the treatment for acute poliomyelitis with convalescent serum, mixed serum from three donors was given intralumbarly, intravenously and intramuscularly in doses of from 10 to 20 cc., and this treatment was repeated once on the next day; the total quantity given, varying with the patient, amounted to from 20 to 30 cc. There was no success in sixty-nine cases in the stage of paralysis (mortality, 21 per cent). Of thirty-eight patients treated in the preparalytic stage, fifteen acquired paralyses, which were permanent in eight; thirty-seven recovered, with or without paralysis, and one died with respiratory paralysis. Twenty control cases ran about the same course. It is possible that the serum has a favorable action in the preparalytic stage, considering especially the results obtained with apes, but it must be given early, during the very first hours or days. Early lumbar puncture is indispensable for diagnosis, and hence for successful treatment.

EMERSON, Boston.

PARALYSIS OF THE PHRENIC NERVE IN CHILDHOOD. M. DE BRUIN, Ztschr. f. Kinderh. **51**:45 (May) 1931.

Three cases of diaphragmatic paralysis are reported, two during the course of intrathoracic tuberculosis and one as the result of a birth trauma. It is noteworthy that in the tuberculous cases, there was no distress. The picture in the other case was quite different. Immediately after birth, there was cyanosis with quick breathing, thoracic in type, the affected side moving more than the other. The signs in the lung were those of massive pneumonia or pleuritis. In roentgenograms it was seen that the diaphragm was high on the side affected, and the movement was paradoxical; i. e., the diaphragm went up in respiration. There are seven cases like this reported in the literature, with a history of a severe delivery and the paralysis located on the right side in contrast with diaphragmatic hernia which occurs only on the left. There is a paralysis of the brachial plexus on the same side; the temperature is normal and the general condition good. The prognosis is dependent on the amount of damage, but in most cases the trouble disappears within nine months. There is great danger from pneumonia. In the tuberculous cases, the explanation of the absence of distress, cyanosis and dyspnea, is probably that the pressure of the enlarged glands increases so slowly that the patient can

accommodate himself to it. It is worth while, in a patient with paralysis of the Duchenne-Erb type, to study the action of the diaphragm roentgenologically, to rule out a paralysis of the phrenic nerve.

EMERSON, Boston.

THE BABINSKI REFLEX IN BABIES. B. BENDIX, Ztschr. f. Kinderh. **51**:93 (May) 1931.

This is a study to gain a clear idea as to whether babies respond to stroking of the sole by a plantar or a dorsal flexion of the great toe or of all the toes. In eighty-three cases there was a positive Babinski sign in only 21 per cent, not a fourth of the entire number. Among 101 newly born babies, tested on one day or on several days, the positive reaction was even smaller, 15 per cent. In only two cases did all of the toes respond. There is no evidence that trauma, difficult delivery or prematurity is the cause of a positive reaction, but the fact remains that in some babies it exists. To explain it, one must accept the opinion of some investigators of the central field as valid, who assume that the striatum at this age is not fully developed. The positive test would correspond not to a genuine Babinski reflex but to the reflex movement that Vogt found in diseases of the striatum in adults and that he designated the pseudo-Babinski sign. No evidence of a direct injury of the striatum was found in these babies.

EMERSON, Boston.

THE GRENZ RAYS IN MENTALLY ABNORMAL AND NEUROPSYCHOPATHIC CHILDREN. C. POTOTZKY, Ztschr. f. Kinderh. **51**:170 (June) 1931.

Treatment with Grenz rays in neuropsychopathic and mentally abnormal children is to be used in cases in which the vasoneurotic factor is conspicuous, and the improvement of this factor may cause an improvement in the disturbance as a whole.

EMERSON, Boston.

THERAPEUTIC POSSIBILITIES IN AMAUROTIC IDIOCY. H. VOLLMER, Ztschr. f. Kinderh. **51**:259, 1931.

While prolongation of the life of an amaurotic idiot is not desirable, the influence of therapeutic agents may give an insight into the pathology of the disease. Vollmer found that the peroral giving of calf's liver and brain, raw and in the extract, had no recognizable effect, and injections for one year with an extract of cerebral lipoid caused no improvement. These agents were used on the ground that there may be an abnormal metabolism of lipoids in the brain cells.

EMERSON, Boston.

HEINE-MEDIN DISEASE: POLIOMYELITIS ACUTA ANTERIOR. J. MUNK and H. A. SCHAAF, Nederl. tijdschr. v. geneesk. **75**:715 (Feb. 14) 1931.

In the summer of 1930 small epidemics of poliomyelitis occurred in several parts of Holland. In describing them the authors once more draw attention to the very different clinical pictures under which the disease may manifest itself and the diagnostic difficulties that may arise from it. Also the new aspects of treatment are discussed. Reconvalescent serum could only be given in small quantities; after intralumbar as well as after intramuscular injection of this serum they observed that the paralysis became worse.

VAN CREVELD, Amsterdam, Holland.

A FAMILIAL HEREDITARY FORM OF TUBEROUS SCLEROSIS. J. KOENEN, Nederl. tijdschr. v. geneesk. **75**:731 (Feb. 14) 1931.

Tuberous sclerosis, described for the first time in 1880, by Bourneville, is a fairly rare clinical picture, and the occurrence of this disease in different members of one family is very rare. The author describes such a family. In several cases

the disease began in childhood. In accordance with other authors, he found that in a later generation the first symptoms of the disease appeared at an earlier age.

VAN CREVELD, Amsterdam, Holland.

NEUROLOGIC CONDITIONS IN BABIES. C. DE LANGE, Nederl. tijdschr. v. geneesk. **75**:1882 (April 11) 1931.

In this clinical lecture the author describes the symptoms observed in a number of babies suffering respectively from myeloencephalomeningitis, acute "aseptic" meningitis, syphilitic meningitis and the acrodynic syndrome. In encephalitis in babies the author often observed munching movements. In one case the rapid appearance and disappearance of a masklike expression, pointing to disease of the large basal ganglions, was especially noticed. In discussing the etiology of acute "aseptic" meningitis the possible relation to poliomyelitis (Netter, Wallgren) is mentioned.

VAN CREVELD, Amsterdam, Holland.

PSEUDOGLIOMA OR GLIOMA. W. P. C. ZEEMAN, Nederl. tijdschr. v. geneesk. **75**:2154 (April 25) 1931.

In this clinical lecture the author enumerates the difficulties that may arise in differentiating glioma from pseudoglioma. A pseudoglioma may be caused by infections, congenital malformation, birth trauma or parasites, all not uncommon influences in childhood. In glioma retinae hereditary influences may play an important rôle.

VAN CREVELD, Amsterdam, Holland.

THE CLINICAL SYMPTOMS OF CEREBRAL PARALYSIS IN CHILDREN. C. SCHAAP, Nederl. tijdschr. v. geneesk. **75**:2709 (May 23) 1931.

In investigating cases of cerebral paralysis in children it is often difficult to settle how far the paralysis is congenital (so-called) or acquired. This is explained by the fact that the normal new-born child demonstrates symptoms that at a later age are regarded as typical of cerebral paralysis and that are probably caused by insufficient development of the pyramidal tract. To overcome the difficulties of diagnosis the author compared a number of patients in whom deviations were observed directly after birth or during the first months of life, without any preceding disease, and a number of patients in whom the symptoms of cerebral paralysis appeared after a disease, usually accompanied by convulsions. In this way he came to the following conclusions: In so-called congenital paralysis the whole extremity is more or less affected; in the acquired cases one distinctly finds deviations originating from one center. In so-called congenital paralysis there exists in the majority of cases paralysis of either one or both limbs. It is difficult to explain this localization by a fetal encephalitis.

VAN CREVELD, Amsterdam, Holland.

Diseases of the Eye

A CASE OF DERMO-FIBRO-LIPOMA OF THE CONJUNCTIVA ASSOCIATED WITH OTHER CONGENITAL ABNORMALITIES. H. B. STALLARD and P. P. MARTIN, Brit. J. Ophth. **15**:580 (Oct.) 1931.

The patient was a boy, aged 3½ years. There was no family history of a congenital anomaly of the parents on either side. In the right eye there was a pinkish-yellow, faintly lobulated swelling extending from the upper to the lower fornix, nearly to the outer canthus and to within 4 mm. of the limbus, except at a position corresponding to 8 o'clock, where a tonguelike process reached the limbic margin. The surface was smooth, with fine hairs projecting from it. The eye was converged. This condition proved to be mechanical, as it disappeared

on removal of the growth. There was marked facial asymmetry, the face being flattened over the right side of the lower jaw, and it seemed on palpation that the junction of the body and the ramus of the mandible on the right side was represented by a gradual curve instead of an angle. There was an accessory auricle situated immediately anterior to the lobule of the right ear. The auricle was well formed, but the external auditory canal was covered over by skin, which extended from the tragus to the concha. A roentgenogram showed the temporary teeth all erupted and normal in number. None of the permanent ones had erupted in either jaw, but the lower first molars were on the point of breaking through. There was a marked asymmetry of the lower jaw, the right side being smaller and less developed than the left. The growth was excised. The histologic diagnosis was dermofibrolipoma of the conjunctiva.

ZENTMAYER, Philadelphia [ARCH. OPHTH.].

THE STRUCTURE OF THE CEREBRAL VISUAL CENTER IN CONGENITAL ANOPHTHALMOS. G. COSMETTATOS, Arch. d'opht. **48**:282 (April) 1931.

In a previous report the author described the structure of the different ocular residua in a case of congenital anophthalmos. The present paper deals with the histology of the visual cortex in the same case. The numerical study of the cells in the calcarine area of the brain of a patient with anophthalmos and its comparison with those in a normal case showed that except for the first three layers, which contain fewer triangular cells, and the third layer, which has a scarcity of cells, the remaining areas do not differ in structure from the normal. There is also a slight diminution in the size of the first and second layers and especially the third. In the case reported, the layer of Gennari appeared normal in contradistinction to the reports of other writers. In the external geniculate bodies, the author found the multipolar cells scarce and small, the majority not having reached their full development. The optic tracts and chiasm were reduced to atrophic ribbons free from nerve fibers.

The author discusses his case in relation to those reported by Leonowa, Hanke, Henschen, Bergen, Bolton, Treipel and Lenz. The relationship between the calcarine area of the brain and the retina is also discussed.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

INFANTILE MYOPIA. A. BRÜCKNER and A. FRANCESCHETTI, Arch. f. Augenh. **105**:1, 1931.

The authors describe twenty-five cases of high myopia in childhood, which they separate as a distinct type from the myopia that increases during school age. They term the condition in the cases under consideration "infantile myopia." Two thirds of the cases occurred in boys and only one third in girls. All the children were about the beginning of the school age, i. e., from about 6 to 7 years old. They showed a myopia that ranged from 3 to 25 diopters and a myopic astigmatism ranging from 1 to 4 diopters.

The following ophthalmoscopic picture the authors regard as typical: The papilla is regularly oval and bordered on the temporal side by a small conus, which seldom exceeds more than a third of the diameter of the papilla. Occasionally, beyond this, there is an area of peripapillary atrophy of the pigment epithelium. The pigment epithelium is largely absent between the papilla and the macula and, in fact, throughout the whole posterior pole of the eye. The pigment in the macular region, however, is increased, so that a dark pigmented spot is characteristically found. The retinal reflexes are characterized by their absence, and the blood vessels show little light streaks.

The visual acuity of these eyes was never normal even with the best correction, and as one would suppose, the higher the myopia the poorer the vision. The visual fields and the dark adaptation were within normal limits. A distinct hereditary influence could be traced in only a few of the cases. For the most

part, the parents were not near-sighted, nor were other children in the same family. The authors could say little of the rate at which the process developed. One patient who had been observed for eighteen years showed practically no change in refraction from a myopia of 9 diopters. On the other hand, one patient showed an increase of 11 diopters over a period of twenty-one years. It could be said with certainty that the increase in myopia had little to do with the use of the eyes. Practically all exogenous factors could be ruled out. The authors consider the myopia as strictly axial, since no change in the curvature of the corneal surface and no evidence of changes in the lens curvature or of indicial myopia were found. They regard the characteristic pigmentary changes in the back of the eye as having something to do with the development of the myopia, but in just what way they are not sure. They voice the opinion that the pigment changes are not the result, however, of stretching of the ocular coats.

ADLER, Philadelphia [ARCH. OPHTH.].

TWO CASES OF LYMPHANGIOMA OF THE CONJUNCTIVA AND OF THE BUCCAL MUCOSA. O. SCHOEPFER, Klin. Monatsbl. f. Augenh. **86**:336 (March) 1931.

Lymphangioma of the conjunctiva is a malformation, usually congenital and mostly located in the conjunctiva of the globe. Two cases of this type in girls, aged 15 and 20, respectively, are reported in this paper. The right eyes were afflicted and amblyopic; extensive lymphangiomas of the mucous lining of the right side of the mouth were present, crossing the median line slightly. This coincidence prompted the author to believe that the malformations developed in early life, and that the conjunctival and buccal lymphangiomas were originally one, but separated at the time when the maxillary and frontal processes developed. The occurrence of orbital defects coupled with cleft palate trends supports this view. The diagnosis is facilitated by the presence of multiple changes. The histologic examination of both cases showed cavernous lymphangioma. The vacuoles were covered with a single layer of flat endothelial cells and were filled with a finely granulated mass, containing no cells and staining faintly with eosin.

STOLL, Cincinnati [ARCH. OPHTH.].

CALCIUM THERAPY IN PHLYCTENULAR DISEASE OF THE EYE. M. CREMER, München. med. Wchnschr. **78**:1223 (July 17) 1931.

A series of 150 cases of phlyctenular disease in children was divided into two groups. The same general care was given to the patients in both groups, but in one group they were given calcium gluconate by mouth, in addition. The average duration of the condition in calcium-treated patients was 14.1 days, while the average in the noncalcium-treated group was 22.5 days. During a period between 9 and 22 months later, about 100 of these children were reexamined. Relapses occurred in only 8 per cent of those having received calcium therapy, while 14 per cent relapses were found in the other group. The author believes that calcium therapy is indicated in phlyctenular keratitis, as it shortens the acute period and militates against relapses to a greater degree than other methods.

MAYER, Chicago [ARCH. OPHTH.].

Diseases of the Ear, Nose and Throat

PARALYSIS OF THE ABDUCENS NERVE ACCOMPANYING A CASE OF MASTOIDITIS: AN UNUSUAL FORM OF GRADENIGO'S SYNDROME. E. MARTIN FREUND, Arch. Otolaryng. **13**:717 (May) 1931.

In 1904, Gradenigo described a syndrome characterized by paralysis of the external rectus muscle supplied by the abducens nerves, unilateral pain in the temporoparietal region on the same side and the presence of otitis media on the effected side. He gave the following as its usual course: "1. The condition

more often occurs in younger patients. 2. The otitis media is usually, though not always, acute and is commonly accompanied by mastoiditis. 3. The tympanum may or may not be perforated. 4. Diplopia sets in suddenly about a month after the onset of symptoms of the middle ear. 5. Optic neuritis is usually absent. However, when present, it indicates a coincidental infection of the optic nerve. 6. About two months after the onset of the otitis media, particularly following surgical intervention, the pain and diplopia disappear. 7. Occasionally, though rarely, diffuse meningitis becomes established, and the case then ends fatally."

The route of infection or involvement of the abducens nerve may be: "(1) the sublabyrinthine route, extending from the tympanum below the labyrinth and internal auditory meatus to the petrous tip, (2) by way of the carotid canal, through erosion of the anterior tympanic wall or through the caroticotympanic formamen, which gives passage to the carotid branches of the tympanic plexus; (3) through the petromastoid canal, the infection extending from the mastoid antrum through the subarcuate fossa, passing inward beneath the semicircular canal, the infection thus reaching a layer of cells that sometimes lies above the internal auditory meatus and eventually locating at the petrous tip; (4) through a layer of cells extending along the eustachian tube, thus passing from the tympanum to the tip."

Gradenigo's syndrome develops during the course of a mastoid infection, but usually manifests itself before the operative stage of the mastoid, although many cases follow operation. Many patients will recover without operation, but the syndrome is usually an indication in itself for a surgical procedure. The prognosis is potentially grave. However, if no complications arise within a week, recovery is the rule. Streptococcus meningitis is the most usual complication and ordinarily is rapidly fatal.

Treatment other than the mastoidectomy is mostly general and symptomatic. A blood transfusion has been found to be beneficial, as it tends to overcome bacterial infection and often aborts a septic sinus thrombosis. Lumbar puncture is dangerous and, unless there is a definite indication for it, is better omitted. An interesting case is reported.

BARNETT, Chicago.

CAVERNOUS SINUS THROMBOSIS IN A CHILD FOLLOWING TONSILLECTOMY. M. C. COMER, Arch. Otolaryng. **13**:733 (May) 1931.

Cavernous sinus thrombosis from furuncles of the upper lip or nasal vestibule is met with fairly frequently, but is rare following infection of the throat. A case is reported which followed tonsillectomy when the operation was performed in the presence of a mild throat infection. It proved fatal in six days.

BARNETT, Chicago.

ADENOIDECTOMY UNDER LOCAL ANESTHESIA. ROY F. NELSON, Arch. Otolaryng. **13**:834 (June) 1931.

A technic for adenoidectomy under local anesthesia is described. Local anesthesia is first applied to the throat. The nasal turbinates are then shrunken and the anesthetic is injected into and around the adenoids, made visible through the nose by this procedure. Complete anesthesia is possible, and removal can follow by any method that the operator cares to use.

BARNETT, Chicago.

THE RÔLE OF THE TONSILS AND THE NASAL ACCESSORY SINUSES IN NEPHRITIS. ARTHUR PALMER, New York State J. Med. **31**:1069 (Sept. 1) 1931.

"Seventy-five per cent of all primary foci are to be found above the larynx." A questionnaire was sent to 989 consecutive patients six months after tonsillectomy. Nineteen of the 523 who replied had suffered from nephritis, and in 11 of these the kidney condition was improved or cured. The ages of all are not given, but one girl aged 5 years recovered from pyelitis.

AIKMAN, Rochester, N. Y.

INVOLVEMENT OF THE EAR IN TOWER HEAD. H. BRUNNER, Monatschr. f. Ohrenh. **65**:1021 (Sept.) 1931.

In the introduction Brunner points out that neither the definition nor the etiology of tower head is quite clear as yet. He then reviews the literature on pathologic conditions of the ear in persons with tower head and shows that the results are again contradictory. He himself examined a large number of children with tower head, and he emphasizes that he never observed signs of involvement of the internal ear, but quite frequently noted adenoid growths and therefore diseases of the middle ear. To prove his theory that tower head more often influences the middle ear and not the internal ear, he describes a case of tower head in which the temporal bone was microscopically examined. In the conclusion he states that in cases of tower head there exist various abnormalities in the region of the middle ear, especially hyperostoses of the bony walls. The latter can be so extensive that they cause displacement of the antrum. It is probable that these hyperostoses have the same cause as the tower head and are therefore coordinated with it. Sequelae of tower head or of the increased cerebral pressure connected with it are to be found in the peaklike tapering of the upper pyramidal edge. However, the membranous internal ear and the bony capsule of the internal ear show no changes. The narrowness of the internal auditory canals and the defective pneumatization of the temporal bones can be grouped together with the tendency to form hyperostoses. Considering the multiformity of the etiology of craniostenosis and the diversity in the timely beginning of the ossification of the suture, it is not surprising that the temporal bones do not always show the same changes. However, it is noteworthy that clinical observation gave essentially the same results as microscopic examination in the case reported.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

USE OF A NEW ARTIFICIAL PALATE IN PALATOGRAPHIC TESTS ON STAMMERERS. F. GUMPERTZ, Monatschr. f. Ohrenh. **65**:1095 (Sept.) 1931.

By using celluloid palates Gumpertz was able to make palatograms that resemble those of the natural palate. Thus he was in a position to compare palatograms of the same sounds produced by the same person at different times, and he could also study the modification of the formation of certain sounds by neighboring sounds. The use of this method on stammering children revealed the following: The sites of articulation and the positions of the tongue for the various sounds are less constant in the stammerer than in the normally talking person. The stammerer soon shows articulatory fatigue. Whereas the pressure of the tongue in the normal adult is symmetrical on both halves of the palate, the unsteadiness in the sound formation by the stammerer is frequently characterized by a greater pressure of one side of the tongue and by wider apposition of the tongue to the palate. Acoustically this asymmetry is not expressed; especially in the s sound it does not necessarily have to be heard as a lateral sigmatism. The palatogram shows still other anomalies in the stammerer that are not perceptible with the ear: for instance, in one case, a tendency to planelike apposition of the tongue in enunciation of t and in another case an s-like position of the tongue in enunciating t. In cases of so-called kappacism one hears instead of k, a t or a t-like sound; yet the palatogram already shows the lingual positions of articulation characteristic for k. These occur either alone or with simultaneous articulation of t. The intermediate sound between k and t can have just as well a t articulation on the soft palate, as a k articulation on the anterior portion of the hard palate. The kappacism of the stammerer resembles in regard to its articulation the intermediate sounds of certain dialects. The transition from t to k is changeable in regard to sound value as well as palatographically. The fact of k articulation in apparent speaking of t is, just as the medially closed n-line in stammerers with medically gaping t-palatogram, a proof that stammering a sound is not merely a mechanical incapacity but is a speech habit. That

an intended t in an isolated syllable is formed atypically, but in a polysyllabic sound combination or as substitute for an intended k is formed typically, likewise is a manifestation of a speech habit. In the stammerer the articulation of the consonants is influenced not only by the articulation of the adjoining vowel (contact assimilation), but by the consonant at the beginning of the following syllable (distant assimilation). The t-palatogram may be influenced by a following p; the k-palatogram may become practically identical with the t-palatogram if a t follows. However, a modification of the articulation of k by a following p or f is not demonstrable. A preceding n in the combination nk does not tend to palatalization, i. e., to forward shifting and amplification of t characteristics; even if palatalization does exist in the nk combination, the k characteristics are often more pronounced than in an isolated k. In stammering that is due to organic factors the assimilation tendency, as observed in the developmental stammerer, is absent. When nd and nt were intended in a case of organic stammering, ng and nk were heard, but the palatogram revealed the line corresponding to the dental n, whereas this line was absent when the posterior n was normally formed i. e., when ng and nk were intended. In the conclusion the author expresses the opinion that contact assimilation in the organic as well as in the developmental stammerer is not merely the result of simplification of movements in accordance with the mechanical principle of least exertion, but is primarily psychologic.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

IRRITATIVE CONDITIONS OF CRYPTS OF PALATINE TONSILS (LATENT CRYPT TONSILLITIS). B. THIESBÜRGER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **28**:459 (Aug. 20) 1931.

Thiesbürger reports studies on the palatine tonsils. His observations are summed up as follows: 1. Systematic studies on sections of clinically and anamnestically healthy tonsils of corpses revealed an unusually high percentage (71) of cases with simple inflammation of one or several crypts. 2. Even normally there are differences between the bacterial flora of the tonsillar crypts and of the surface of the tonsils, and this observation could be corroborated in studies on living persons. The conditions are similar to those in the case of appendicitis. The flora of the crypts even normally contains those micro-organisms which cause the clinically manifest forms of acute and chronic tonsillitis, and the clinically latent inflammations of the crypts. 3. In many cases of clinically latent inflammations of the crypts, a phagocytosis of certain micro-organisms by the leukocytes takes place simultaneously. This phagocytosis is the only sure sign of the pathogenicity of the micro-organisms in each respective case. Moreover, the bacterial phagocytosis is also a significant basis for the correct evaluation of the bacterioscopic and bacteriologic findings. 4. The author defines the clinically latent crypt tonsillitis. He maintains that not the macroscopic appearance of the tonsillar plugs, but rather the microscopic detection of more or less marked leukocyte admixture is decisive for the diagnosis of inflammation of the crypts. 5. Investigations with a combination of several methods justifies the assumption that diplostreptococci, especially hemolytic streptococci, are the main cause not only of the clinically latent crypt tonsillitis but also of the clinically manifest forms of acute and chronic tonsillitis. Judging by appearances, the specific tonsillitis, at least the Plaut-Vincent type, begins with a transitory streptococcic tonsillitis. 6. The essential cause of tonsillitis is either an increase in the virulence of the bacteria or a decrease in the resistance of the organism. As predispositional factor, the stagnation of the cryptic contents is of primary importance in the development of the inflammation of the crypts. As probable factors that are responsible for the prolongation of the process, the author considers horny plugs, cornification and perhaps also tonsilloliths, but he does not hold leptothrix nodules responsible. 8. It is very probable that the clinically manifest forms of tonsillitis begin with clinically latent, acute inflammations of the crypts.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

ACUTE INFLAMMATION OF THE MIDDLE EAR DURING CHILDHOOD. M. MEYER, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:217 (July) 1931.

Meyer reports the clinical observations on 200 nurslings and children with acute otitis who came under his observation in the last two years. He discusses the local symptoms, the general reactions of the organism, the pathologico-anatomic findings, the various forms that otitis assumes and the treatment. He found that the clinical aspects of acute otitis are much the same in nurslings, older children and adults, and he considers it unnecessary to make differentiations merely on the basis of age. The age of the patient is only one of many points that he thinks deserving of consideration. The difficulties in the estimation of otitis media in children, even when the technical difficulties in the examination are disregarded, are, on the whole, greater than in later life. This is mostly due to the frequency of intercurrent diseases, which mask the symptoms of the ear disease. Another peculiarity of otitis media in children is that it is difficult to classify and for this reason each case demands individual observation.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

NORMAL AND PATHOLOGIC EARS OF NURSLINGS AND CHILDREN. M. MEYER, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:283 (July) 1931.

In the first part of the article Meyer discusses the symptomatology and the results of the microscopic investigations in cases of mucous-suppurative mastoiditis. Then he evaluates Preysing's theory that the hollow spaces that develop in the middle ear of nurslings during otitis represent a pneumatization process. Although most investigators have refuted Preysing's theory, the author concludes from his own observations that the hollow spaces are the product of an abnormal pneumatization process, and he agrees with Preysing, who designated them as "hollow space sprouts." In the third part of the article he discusses the transformation of the medullary spaces during pneumatization. In the summary he states that the extension of the embryonal connective tissue from the antrum into the medullary spaces can be explained without the actual ingrowing of the embryonal connective tissue, especially since this tissue is in a state of retrogression after birth. Even if it cannot be proved morphologically, it appears nevertheless probable that the connective tissue, which resembles the submucosa, becomes visible in the medullary spaces because the cellular constituents of the lymph marrow retreat. The transformation into fiber marrow or into fat marrow then takes place much like in other bones, only for the local peculiarity that in the mastoid process air spaces are formed by the epithelial activity.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

SO-CALLED OTOGENIC, ACUTE, PROGRESSIVE OSTEOMYELITIS OF THE TEMPORAL BONE IN CHILDREN. W. BROCK, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:295 (July) 1931.

Brock states that acute otogenic progressive osteomyelitis of the temporal lobe is extremely rare in children. He gives a short review of the literature and then describes a case that came under his observation. In order to gain a better understanding of the etiology and pathogenesis of this disease, he made a careful postmortem examination, and the temporal bone was subjected to careful histologic examination. He also discusses the theories of pathogenesis that have been advanced by other authors and concludes that his theory of pathogenesis is still hypothetic in that he has no definite clinical and anatomic proofs. Since the cases are extremely rare, one otologist rarely having occasion to observe several, the author advises the exchange of observations on cases of this nature.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

CLINICAL AND PATHOLOGIC EXPERIENCES IN OTITIS MEDIA DURING CHILDHOOD. W. UFFENORDE, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:308 (July) 1931.

Uffenorde first calls attention to the chronic inflammation of the auditory tubes which is frequently observed in children. He found that this condition was refractory to most therapeutic measures, but also observed that paracentesis of the tympanic membrane usually improved the hearing capacity, at least as long as the perforation was kept open. However, as soon as the opening closed, the audition became impaired again. All the therapeutic measures that are employed in exudative diathesis the author considers advisable, in that most of these children are subject to it. Relapses of the auditory disorder are quite frequent, and it is probable that local factors such as a hypertrophy of the peritubal cells are the cause of the prolongation. Also worthy of consideration is the fact that in many cases the pneumatization process is completely inhibited. A permanent improvement often does not set in until after puberty, when the general condition and the resistance have improved. Another aspect of otitis media, to which the author calls attention, is a sudden swelling behind the ear in children in whom previously there were neither auditory disturbances nor a discharge from the ear. He does not consider this swelling as a manifestation of a primary mastoiditis, but rather thinks that this proves that the tympanic membrane has often more resistance than the thin bony closure toward the antrum. In cases of this nature, paracentesis is advisable. Although otitis media usually takes a harmless course during the nursling age, the author warns that pediatricians should not underestimate its seriousness and consider paracentesis as unnecessary, for of 692 children with otitis media who came under his observation, 329 had to undergo paracentesis and in 151 antrotomy had to be resorted to. Further, the histologic observations on the petrosas of 12 young children are discussed: It was found that the most common form of otitis in nurslings is the simple, suppurative exudative inflammation. The process does not differ from that observed in adults. In the last part of the article, the author shows how in nurslings the closed otitis media leads to labyrinthitis.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

FAMILIAL OCCURRENCE OF INFLAMMATORY DISEASES OF THE MIDDLE EAR. H. RICHTER, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:319 (July) 1931.

After reviewing the literature, Richter shows on genealogical trees that inflammatory diseases of the middle ear, especially chronic suppurations, may be hereditary. These inflammations of the middle ear, which develop as the result of an inferior organ constitution, may be passed on uninterruptedly or may occur sporadically. There is no marked difference in the behavior of the two sexes. The slightly higher incidence in man can be accounted for by exogenic factors. It is further pointed out that persons who are affected with hereditary aural diseases usually show also other defects. The author calls attention to the great frequency of tuberculosis in the families in which aural diseases are hereditary. Because of the close relationship between ear and nose, and ear and nasopharynx, pathologic changes in these regions, particularly the hyperplastic forms of the pharyngeal lymphatic ring, should be watched for. The family anamnesis and general habitus of a patient with aural disease should be given consideration, because the information thus gained will be helpful for the prognosis.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

SURGICAL TREATMENT FOR EAR DURING EARLY CHILDHOOD AND PNEUMATIZATION DEVELOPMENT. H. LOEBELL, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:326 (July) 1931.

In order to learn the later fate of children who had undergone antrotomy during early childhood, Loebell studied the development of pneumatization of the mastoid

process by means of roentgenoscopy. A tabular report shows the results of the examinations in 20 cases. In 14, that is, in two thirds of the cases, the pneumatization was inhibited, particularly on the side that had been operated on; in the other 7 cases it was normal. In reviewing the results of several other workers who have investigated this problem, he found that their conclusions contradicted each other. He thinks that this is due to the fact that most investigations were made on a comparatively small material, and he therefore considered it advisable to study the normal pneumatization process on those persons who had not had otitis media during childhood or in adult life and also on persons who had had otitis in later life, after pneumatization had been completed. Investigations on 100 cases revealed that in 23, that is, in more than 20 per cent, there was a marked inhibition of the pneumatization. This indicates that the inhibited pneumatization cannot be considered as the result of otitis media and of antrotomy, and the author thinks that more investigations, roentgenologic as well as histologic, will be necessary to solve the problem of pneumatization. Observations on 25 patients with ozena revealed in 11 of them a normal pneumatization; in 14 there was a bilateral inhibition.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

CHRONIC TONSILLITIS AND CHRONIC TONSILLOPATHY. A. LINCK, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:342 (July) 1931.

According to Linck, the term "chronic tonsillitis" is applied to a permanent pathologic condition of the palatine tonsils. It is an empiric term, and it was selected because, on the basis of clinical observations, it was assumed that it was always due to chronic inflammatory changes of the palatine tonsils. However, careful investigations revealed that the pathologico-anatomic collective term "chronic tonsillitis" is not applicable to some tonsillar diseases, and therefore the term "chronic tonsillopathy" was recommended. The term chronic tonsillopathy includes those conditions that are usually termed chronic tonsillitis, but the two terms are not synonymous. Tonsillopathy is the more general term including also those pathologic conditions of the tonsils in which inflammation is absent. In the main part of the article the author discusses first the pathology and then the clinical aspects of the various forms of chronic tonsillopathy, and he discusses particularly the therapeutic and prophylactic significance of tonsillectomy.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

Surgery and Orthopedics

UROLOGY IN CHILDREN. FREDERICK J. PARMENTER, New York State J. Med. **31**:689 (June 1) 1931.

The author calls attention to the improved methods of diagnosis and treatment in urology, especially in renal infections, dysuria, congenital defects and functional nocturnal enuresis. While iopax is of great value, it "cannot take the place of the cystoscope and ureteral catheter as a routine method of diagnosis."

AIKMAN, Rochester, N. Y.

ACUTE INTUSSUSCEPTION WITH MECKEL'S DIVERTICULUM. L. S. TRASK and S. E. C. TURVEY, Northwest Med. **30**:194 (April) 1931.

In the case reported, the symptoms were the usual ones. The abdomen was distended and tympanitic, but no mass was felt externally or rectally until the fourth day, when a sausage-shaped tumor was felt in the cecal region. The ileum was invaginated into the cecum for a distance of 6 inches (15.2 cm.), and a small Meckel's diverticulum was invaginated into the ileum. It was necessary to perform an ileostomy.

SCOTT, Philadelphia.

CONGENITAL COXA VARA. CECIL P. G. WAKELY, Proc. Roy. Soc. Med. **24**:61 (Nov.) 1930.

A case of congenital coxa vara is reported in a child aged 2 years. The roentgenogram showed the head of the femur which was in the acetabulum. The upper end of the shaft of the femur was definitely bowed, and there was 3½ inches (8.8 cm.) of shortening of the left femur. The child could walk on the toes of the left foot with the pelvis tilted downward.

WILLIAMSON, New Orleans.

INTUSSUSCEPTION IN AN INFANT. JAMES CROOKS, Proc. Roy. Soc. Med. **24**:113 (Dec.) 1930.

A case of intussusception is reported in a girl aged 8 months. The operation is also described.

WILLIAMSON, New Orleans.

A CASE OF TORSION OF THE ADNEXA IN A GIRL OF THIRTEEN YEARS. P. INGELRANS and MINNE, Bull. Soc. d'obst. et de gynéc. **20**:268 (April) 1931.

An abdominal tumor had been present for three months. Because the child was large and well developed for her age, pregnancy was suspected. This was ruled out, and at operation the left fallopian tube was found to be rotated 180 degrees. This was ligated and removed. The left ovary and uterine appendages on the right were found to be normal and were left in place. Convalescence was uneventful.

The authors review the literature, citing forty-one cases that have been recorded, and emphasize the benignity of the symptoms as compared with the gravity of the lesions found at operation.

TURNER, Chicago.

DYSTONIA OF ATTITUDE. L. BABONNEIX and A. MIGET, Bull. Soc. de pédiat. de Paris **29**:72 (Feb.) 1931.

A girl, 8 years old, had an abnormal gait. This began to manifest itself about two months previously by an internal rotation of the right foot. She gradually became worse until she showed an abnormal attitude consisting of a lateral curvature of the trunk with the head carried forward and slightly rotated to the left. The muscles were hypertonic so that there was a stepping character to the gait especially of the right leg. She could not walk rapidly or run, and appeared to fall when she tried to move quickly. When the child was put in dorsal decubitus, all the deformity disappeared and the hypertonic muscles became hypotonic. In the sitting position the neck and trunk assumed the same deformity as when the patient stood up. Neurologic examination showed nothing abnormal. The spinal fluid was not examined.

BENJAMIN, Montreal, Canada.

REVIEW OF SURGICAL AND ORTHOPEDIC MEASURES IN THE TREATMENT OF INFANTS DURING THE YEAR 1931. A. MONCHET and C. ROLDERER, Paris méd. **2**:53 (July 16) 1931.

The authors give their annual review of the progress in surgical procedures for the treatment of infants during the past year. The topics include surgery of the vertebral column, congenital malformations, deformities, obstetric paralysis, tuberculosis and abdominal conditions.

SANFORD, Chicago.

POSTOPERATIVE TREATMENT OF CONGENITAL LUXATION OF THE HIP. J. GOURDON, Paris méd. **2**:71 (July 16) 1931.

Four diagrams of exercises to improve congenital luxation of the hip are given. The next step is to determine the amount of function to correct so that a normal walk can be attempted.

SANFORD, Chicago.

PRIMARY MALIGNANT ADAMANTINOMA OF THE OVARY. M. N. ZAJEWLOSCHIN, Frankfurt. Ztschr. f. Path. **41**:100, 1931.

A primary malignant adamantinoma of the ovary in a girl 8 years old is reported. During the operation for removal, it was noted that both tubes and the uterus were absent. The tumor weighed 200 Gm., and measured 6 by 7.5 by 9 cm. Its surface was in part smooth and in part nodular. On section, the bulk of the tumor consisted of an irregular lobular mass, a small amount of interstitial tissue and some calcified areas. A few cysts were also noted. Histologically, the tumor revealed typical adamantinoma structures. The author believes that the tumor reported is a congenital teratoma in which the predominant portions are represented by the adamantinoma. It is possible that originally this tumor was a dermoid cyst with tooth structures, from which the adamantinoma developed.

SAPHIR, Chicago [ARCH. PATH.].

SO-CALLED FLATFOOT IN CHILDHOOD. HANS SPITZY, Kinderärztl. Praxis **2**:1 (Jan.) 1931.

As a prophylactic measure Spitzy warns against interfering with the normal development of the foot by encouraging the child to stand and walk too early. He advises a long period of creeping and permitting the child to stand only of its own volition. The free development of the musculature of the toes and the foot should not be retarded by wearing shoes too early. When shoes become necessary, those with soft leather soles, similar to moccasins, should be recommended. For the treatment of flatfoot, inserts in the shoe to prop up the weakened arches should never be employed. They are not only of no benefit, but like the old-fashioned braces for round shoulders, may do positive harm. Spitzy advises the insertion of a button in the inner aspect of the child's shoe; the discomfort caused by the button causes the child to walk awkwardly at first, but in a few days without conscious effort he is curving his foot outward and walking correctly by the use of his own muscles.

HUENEKENS, Minneapolis.

THE TREATMENT OF EMPYEMA IN INFANCY AND EARLY CHILDHOOD. HERMANN FLESCH, Kinderärztl. Praxis **2**:99 (March) 1931.

Flesch emphasizes the high infant mortality in empyema when rib resection, thoracotomy, closed drainage and simple aspiration are used. He suggests the further trial of two other methods, viz., irrigation with 5 per cent ethylhydrocupreine solution, after simple aspiration, and autopyotherapy. The latter method consists of repeated aspiration and the reinjection of from 0.25 to 1 cc. of the aspirated pus subcutaneously. His results with these methods are encouraging, though not startling. He emphasizes the necessity for individual treatment and methods in each case.

HUENEKENS, Minneapolis.

MALIGNANT TUMOR OF THE CERVIX IN AN INFANT. F. KOHLHAAS, Monatschr. f. Geburtsh. u. Gynäk. **86**:58, 1930.

A malignant tumor of the cervix was noted in a child, aged 16 months, who died of bronchopneumonia. At the age of 6 months, bloody vaginal discharges were the first indications of disease, and thereafter bleeding of several days' duration recurred at intervals of three or four weeks. At autopsy, metastases were found in the para-aortic lymph glands, the liver, the right lung and the right bronchial lymph nodes. The primary tumor had perforated the right common iliac vein, which was thrombosed. The pelvic tumor growth had also compressed the bladder and ureters, so that a large bilateral hydronephrosis resulted. The tumor cells resembled epithelium, and had large, lightly stained nuclei and a large amount of cytoplasm. Some cells were spindle-shaped and resembled fibroblasts. The picture was not that of a pure carcinoma, and much less that of a sarcoma, so that a diagnosis of an immature malignant tumor was made.

RUSTINAT, Chicago.

THE TREATMENT FOR EMPYEMA IN INFANCY AND CHILDHOOD. C. STAMM, Monatschr. f. Kinderh. **49**:11 (Jan.) 1931.

The prognosis of empyema depends on the age of the patient, being more favorable in the older child. In thirty cases occurring during the first years of life only eleven of the patients were cured. Of twelve patients from 3 to 12 years of age, eleven were cured. Stamm believes that for the first two years the method of puncture is to be recommended unless the pus is too thick, when a thoracotomy must be done. In later childhood, rib resection may be necessary, although puncture should be tried.

GERSTLEY, Chicago.

HERNIA OF THE HIATUS OF THE ESOPHAGUS. E. UNSHELM, Monatschr. f. Kinderh. **51**:94 (Oct.) 1931.

Hernia of the hiatus of the esophagus occurred in a 9 months old baby. An effort was made to close the hernial opening, which was as large as a 3 mark piece. The child died during the operation. Roentgenograms are shown.

GERSTLEY, Chicago.

SIMPLIFIED TREATMENT FOR EMPYEMA IN CHILDREN. C. NOEGGERATH, München. med. Wchnschr. **78**:303 (Feb. 20) 1931.

Noeggerath found that the results following rib resection for empyema were not good; neither was he satisfied with single or repeated aspiration. The old method of simple intercostal incision and insertion of a rubber drain was most desirable for the patient, doctor and nurse.

BRAHDY, Mount Vernon, N. Y.

POSTOPERATIVE HYPERPYREXIA IN INFANTS AND ITS TREATMENT. A. NIELSEN, Ugesk. f. læger **93**:416 (April 16) 1931.

Nielsen describes three cases of hyperpyrexia following minor surgical procedures under short ether and chloroform anesthesia. The cause is taken to be a disturbance of the heat-regulatory mechanism. The patients in two similar cases, treated by external applications of cold and massage of the body surface, recovered.

ELGHAMMER, Chicago.

Miscellaneous

THALLIUM, A DANGEROUS DRUG. EDITORIAL, New England J. Med. **204**:1117 (May 21) 1931.

Thallium, in the form of the acetate, is principally used as a depilatory in the treatment for ringworm of the scalp. The drug also occurs in face creams, sold in the open market, for the removal of superfluous hair. Lynch and Scovell give details of the death of three children aged 10, 7 and 5 years, poisoned by thallium acetate used for ringworm. In another group of children, noted by the same authors, thirteen of sixteen died. Some patients who have not even received a depilating dose have failed to recover from the toxic effects. Like lead, the drug has a special affinity for the nervous system, and nonfatal cases usually show peripheral neuritis, largely motor in type, with atrophy, or evidence of structural damage to the brain, and mental disease or a striatal syndrome. Recovery is slow, but tends to be complete. Apparently the margin between a depilatory and a toxic dose is extremely small, and allows for no idiosyncrasies. The author believes that the public and physicians should be warned against its use.

GENGENBACH, Denver.

A Study of Illness Among Grade School Children. C. C. Wilson, I. V. Hiscock, J. H. Watkins and J. D. Case, Pub. Health Rep. **46**:1801 (July 31) 1931.

These studies were made on the school children of New Haven for the period from January, 1927, to June, 1928. The school attendance was approximately 27,000, according to the 1920 census. Fifty-three and eight tenths of all cases of sickness were due to respiratory disturbances, as were 38.9 per cent of the total number of days of sickness. Contagious diseases caused 27.9 per cent of the cases and 44.2 per cent of the total number of days of sickness. Whooping cough caused the longest absences, averaging 49.3 days, and scarlet fever was next with 31.7 days. The average number of days of sickness was greatest for the 5 year old group. The days of sickness per case showed no sex differences.

Sanford, Chicago.

Current Prevalence of Communicable Diseases in the United States. Pub. Health Rep. **46**:1871 (Aug. 7) 1931.

For the period of June 21 to July 18, 1931, the number of cases of poliomyelitis had increased to more than twice that for the same period the previous year. The states on the Atlantic Coast and the East North Central group were most affected. The typhoid fever rate was also double that for the preceding four week period. All other contagious diseases showed a decrease. The general mortality was 11.2 per thousand; the previous year it was 10.8.

Sanford, Chicago.

Provisional Birth, Death and Infant Mortality Figures, Birth Registration Area, 1930. Pub. Health Rep. **46**:2372 (Oct. 2) 1931.

For the birth registration area (exclusive of Utah) the birth rate for 1930 was 18.9, the same as that for 1929. The highest birth rate was 28.5, for New Mexico, and the lowest 14.1, for Oregon. The death rate was 11.3 for 1930, 0.6 lower than for 1929. The highest death rate was 15.5, for New Mexico, and the lowest 7.9, for North Dakota. The infant mortality of 64.2 for 1930 was the lowest since the establishment of the registration area in 1915. The highest rates were 144.9, for New Mexico, and 116.2, for Arizona. The lowest were 48.4, for Washington, 49.2, for Nebraska, and 50, for Oregon.

Sanford, Chicago.

Treatment of Children at the Seaside (Excluding Surgical Tuberculosis). Carl Häberlin, Brit. M. J. **2**:331 (Aug. 22) 1931.

The author stresses, from both a practical and a historical point of view, the benefits to be derived from sea air for children suffering from respiratory catarrh, malnutrition, gastro-intestinal conditions (especially if prolonged), diseases of the cardiovascular system, rheumatism, nervous disorders, etc. He feels, however, that a period of from three to six months or maybe longer is necessary, and that the climate must not be changed to any other during this time. He issues a definite warning, however, with regard to sending children who are not well to the seashore without previous medical examination or without being observed at the seashore by a physician. He states that many children either come to the seashore without medical advice or are just told by physicians to take a sojourn at the seashore without their real condition being known. This is not good for the child since children who are not normal from any cause must become acclimated gradually to both sunshine and water.

Royster, University, Va.

The Adaptation of European Women and Children to Tropical Climates. A. Castellani, Proc. Roy. Soc. Med. **24**:1319 (July) 1931.

The climate of the lowlands of the tropics is not suitable for the great majority of European men, women or children. Children 2 or 3 years old stand the climate well, although teething, speech and walking may be retarded. After this they do

not do well, and look pale and weak. Children should be sent home at not later than 8 or 10 years of age on account of danger to the nervous system and sexual precocity. They should not be allowed to return until they are 20 years old.

SANFORD, Chicago.

SOME ENDOCRINE DYSFUNCTIONS IN CHILDREN REPRESENTED IN ART. G. MAZZINI, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 689.

This is a chapter of a book by Mazzini that is about to be published, entitled "Il bambino nell' arte visto da un medico." Three paintings are reproduced. The first is at Mantova in the bridal suite of the famous castle; Andrea Mantigna has painted the family of Ludovico Gonzaga and his bride Barbara of Brandenburg, grouped on a porch; among them is little Cecilia, the court dwarf, affected with infantile myxedema. The second is at the City Museum at Vicenza and by an unknown artist. It is entitled "Parvula" (little child). The child is a complete dwarf (microsomia). The third is by Ignazio Zuloaga and is shown at the Luxembourg Museum in Paris. It is entitled "Nana," and is a portrait of a girl with hypopituitarism of the adipose type.

HIGGINS, Boston.

THE PROTECTING GODDESS OF MATERNITY AND OF INFANCY AMONG THE ANCIENT ETRUSCANS: MATER MATUTA. R. SIMONINI, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 694.

The Etruscans represent the earliest established civilization of Italy. Their origin is unknown, but may have been from the northern (Germanic) tribes; their religion and gods, however, for the most part come from the Egyptians and Greeks. Mater Matuta, spoken of by the Romans as Goddess of Dawn or the Morning, was considered by the Etruscans as protecting deity of maternity; Portunus, her son, is the protector of childhood. Mater Matuta and Portunus correspond to the Egyptian deities, Iside and Oro, and to the Greek deities Leucothea and Palaemon.

HIGGINS, Boston.

COMPARATIVE STATISTICS CONCERNING THE MORBIDITY OF INFANTS AND PRESCHOOL CHILDREN IN FOSTER HOMES AND IN INSTITUTIONS OF MUNICH. O. ULLRICH, E. ULLRICH-AYER and E. G. WESTENDORFF, Gesundhfürs. f. d. Kindesalt. **6**:157 (June) 1931.

The authors, who are pupils of Pfaundler, have studied the morbidity of children in institutions, and compared it with the morbidity of children of the same age in their own or foster homes. The results emphasize the value of Pfaundler's program, which calls for the individual care of children, attempts to reduce as far as possible the duration of their stay in the hospital and requires the separation of infants from older children in all institutions. They also regard the development of many small institutions as preferable to concentration in one large institution. The statistics show that the morbidity of children in institutions increases in indirect proportion to the age of the children and that the presence of preschool children endangers the health of infants; the larger the institution, the higher is the morbidity.

REICHLE, Cleveland.

THE USE OF MORTALITY LISTS IN SOCIAL SERVICE WORK AMONG INFANTS. KARL MOSSE, Gesundhfürs. f. d. Kindesalt. **6**:190 (June) 1931.

The careful observation of mortality lists is of great value to any field worker. The author cites specific cases to bear out this statement.

REICHLE, Cleveland.

Society Transactions

CENTRAL STATES PEDIATRIC SOCIETY

Sixteenth Annual Meeting, Oct. 16 and 17, 1931

Friday Morning, Oct. 16, 1931

THE DETECTION OF VITAMIN A BY ULTRAVIOLET RADIATIONS. DR. ROBERT J. NORRIS, Cincinnati.

The importance of the effect of ultraviolet rays on vitamin A is pointed out from the standpoint of the widespread irradiation of oils and foodstuffs to increase their vitamin D content. Destruction of the activity of vitamin A by irradiation, as assayed biologically, was found to proceed rapidly after an initial induction period, in which there was very slight or no inactivation. The colorimetric assay, with antimony trichloride, did not agree with the biologic assay.

NEWER METHODS IN THE TREATMENT OF HEMOPHILIA. DR. C. A. MILLS, Cincinnati.

Dr. Mills discussed the usefulness of theelin, together with its limitations, in hemophilia. The results of certain other newer methods of treatment were presented.

BRONCHIAL LAVAGE. (Illustrated with moving pictures.) DR. H. L. STITT, Cincinnati.

Dr. Stitt described a method of treating patients with chronic bronchitis, bronchiectasis and abscesses of the lungs. The principle involved is that of drainage to assist in overcoming the impairment of the four natural functions of the bronchi, namely, the cough reflex, ciliary action, autogermicidal action and bronchial peristalsis. This presentation was illustrated with moving pictures.

CONDITIONS IN CHILDHOOD WHICH PREDISPOSE TO THE EARLY DEVELOPMENT OF ARTERIOSCLEROSIS. DR. PEARL ZEEK, Cincinnati (Department of Pathology, University of Cincinnati, and General Hospital).

A study of 1,070 consecutive autopsies on persons under 30 years of age revealed atherosclerosis with far greater frequency in association with lesions of rheumatic heart disease, diabetes mellitus and chronic renal disease than with any other disease conditions. This association was so striking as to indicate emphatically an etiologic relationship.

HARELIP AND CLEFT PALATE. DR. REED SHANK, Cincinnati.

Emphasis was placed on the importance of the time of operation, cooperation between the surgeon and the pediatrician, choice of method of feeding and a later check for malformation.

STUDIES IN RICKETS: V. RELATION OF DIET DURING PREGNANCY TO THE DEVELOPMENT OF THE CHILDREN AT 7 YEARS OF AGE WITH PARTICULAR REFERENCE TO TEETH. DR. J. V. GREENEBAUM and DR. T. K. SELKIRK, Cincinnati (B. K. Rachford Department of Pediatrics, University of Cincinnati, and the Babies Milk Fund Association of Cincinnati).

For the past seven years we have been studying the effect of controlled diet during pregnancy on the incidence and development of rickets. In this work

we have observed the offspring of twenty-five mothers, paying particular attention to their growth, nutrition and teeth. In the present study we are using only the Negro children, seventeen being available. (Accompanying tables and a chart showed in detail the main facts to date.)

During pregnancy the diets of the mothers were arranged and supervised by dietitians from the Department of Nutrition of the University of Cincinnati. It was impossible to bring the caloric intake to a desirable level in all cases, although all the diets were adequate as to mineral salts and vitamins.

After birth the children received routine clinic care under the Babies Milk Fund Association. Some were lost from observation for considerable periods of time. Two years ago (five years after the beginning of the experiment), a study was made of these children, and the results were reported before the American Dental Association. At that time definite proof was lacking that rickets had any effect in producing caries of the deciduous teeth, and that there was any relationship between the prenatal diet of the mothers and the condition of the deciduous teeth of the children.

The present study, which was made after the dental survey, shows several additional interesting relationships in this series which are worthy of comment. There was apparently some relationship between the caloric intake of the mother during pregnancy and the incidence of caries of the deciduous teeth of the offspring; namely, the children of the mothers whose daily diets contained less than 1,500 calories per day had appreciably more caries (83 per cent) than those whose mother's daily intake was greater than 1,500 calories (63 per cent). We have also in this study been able to show a relationship between rickets in infancy with the condition of the deciduous and permanent teeth up to 7 years of age, in that the children who had marked rickets had a greater incidence of caries and twice as many carious teeth per child as those who had had mild rickets in infancy.

ONE HUNDRED CASES OF PREMATURITY. DR. EDWARD A. WAGNER, Cincinnati.

Dr. Wagner reported on a hundred cases of prematurity in which an incubator room that had simple methods to control the temperature and humidity was used. An attempt was made to reduce the high mortality.

Friday Afternoon, Oct. 16, 1931

THE SPEEDWELL PLAN FOR CONVALESCENT CHILDREN. DR. HENRY DWIGHT CHAPIN, New York.

One disadvantage of the hospitalization of infants and little children is that they are often kept too long. They should not only be discharged early, but have some oversight in order to insure permanent benefit. Institutions for convalescents, according to my view, have not been successful in handling this problem. After treatment in the hospital it is better to shift from group to family care.

Twenty-nine years ago I inaugurated the Speedwell plan of carefully systematized boarding out. We operate in what are called units, all of which are distinct, separate and to a certain extent autonomous. The underlying idea of a unit includes a certain area in a city or the country — preferably the latter — that is sufficiently circumscribed to allow workers to become acquainted with the personnel of the neighborhood and is accessible for communication. We are not overfastidious in selecting homes. If the foster mother has maternal instincts and healthy children of her own, a little training will do the rest. A salaried physician and trained nurse are then appointed to take charge of each unit. Careful histories of every child are kept on a card system that is uniform in all units. Admissions are arranged through the Convalescent Service of the United Hospital Fund of New York.

There are now nine units with 244 available beds, serving all the hospitals in Greater New York. There are three specialized units for convalescent work: a Negro unit operating in Harlem, a postcontagious unit for the immediate care of children discharged from the hospitals for communicable diseases of Greater New York and a postcardiac unit for children with beginning endocarditis. The Speedwell plan has demonstrated that the plain American home, by the carefully controlled environment it has inaugurated, can be safely and satisfactorily utilized for much remedial work for children at a cost much less and with better results than an institution.

Sensitization and Desensitization in Tularemia and Brucella Abortus Infections. Dr. William B. Wherry for Dr. Lee Foshay and Dr. Alfred O'Neill, Cincinnati.

A marked hypersensitivity is manifested by human beings, guinea-pigs and rabbits. Sensitization and desensitization influence the clinical course of the disease. Experiments were made on the production of relatively nontoxic antigens for desensitization. The results of desensitization were reported.

Bacterial Asthma. Dr. A. Graeme Mitchell, Cincinnati.

Dr. Mitchell presented an analysis of the results of a study of a group of children with asthma. Complete bacteriologic studies were made of the upper respiratory tracts of children with asthma; their sensitivity to the isolated bacteria was determined by skin tests, and subsequent desensitization was produced by the injection of a vaccine.

Studies in the Etiology of Poliomyelitis. Dr. Merlin L. Cooper, Cincinnati.

A pleomorphic green-producing streptococcus has been isolated from the spinal fluids of a high percentage of patients. This micro-organism, when injected into rabbits, produces flaccid paralysis and death with characteristic pathologic changes in the central nervous system. Convalescent human serum protects against this micro-organism. This presentation was illustrated with moving pictures.

Scarlet Fever Immunization with a Formaldehydized Toxin, Also Combined Scarlet Fever and Diphtheria Immunization with Combined Formaldehydized Diphtheria and Scarlet Fever Toxins. Dr. Robert A. Lyon, Cincinnati.

Dr. Lyon presented an analysis of the results obtained with a combined diphtheria-scarlet fever toxoid in an attempt to produce active immunization against diphtheria and scarlet fever.

Experimental Iritis Associated with Local Sensitization. Dr. A. L. Brown, Cincinnati.

Iritis and uveitis are probably the result of some mechanism that sensitizes the tissues locally. Local ocular anaphylaxis has been produced experimentally with foreign proteins, such as egg white, and foreign erythrocytes. The iris has been sensitized by streptococcus toxin, and iritis has been produced by injecting the same toxin intravenously, ten days later. The toxin has likewise been used to sensitize the iris and uveal tract, and uveitis has been produced by the intravenous injection of the organism.

Diagnosis and Treatment of "Acidosis." Glenn E. Cullen, Ph.D., Cincinnati.

The term "acidosis" is at present often used carelessly as the description of symptoms which may or may not be due to changes in the acid-base balance

of the blood. In diagnosing "acidosis," it is imperative that the alkali reserve be determined, and it is desirable that the p_H be known. True acidosis, i. e., lowered alkali reserve and decreased p_H of the blood, is a condition resulting from various causative factors and is not generally in itself a primary causative agent in disease. Correct treatment can be made only when the acid-base condition of the blood is known and then should be quantitatively proportional to the disturbance.

THE DISTRIBUTION OF PHOSPHORUS IN THE BLOOD. DR. GEORGE MARTIN GUEST, Cincinnati.

The total phosphorus (around 40 mg. per hundred cubic centimeters) of the whole blood may be partitioned as inorganic (from 3 to 5 mg.), the organic acid-soluble (25 mg.) and the lipin (10 mg.). In clinical studies most attention has been paid to the inorganic fraction, commonly known to be low in rickets and high in severe nephritis, to cite but two examples. More complete measurements disclose rather large fluctuations in certain of the organic phosphorus compounds that have received comparatively little study.

RETROPHARYNGEAL ABSCESS. DR. HAROLD G. REINEKE, Cincinnati.

Dr. Reineke stressed the value of the lateral roentgenogram in assisting in the diagnosis of a retropharyngeal abscess.

SOME OF THE ORTHOPEDIC ASPECTS OF THE TREATMENT OF INFANTILE PARALYSIS. DR. JOSEPH A. FREIBERG, Cincinnati.

Dr. Freiberg stressed the importance of the early recognition of all of the muscles involved in the disease. There is an absolute need of a careful, complete examination of the muscles by one trained in this type of work. Some paralyses of isolated muscles are obscured because of the compensation for the weakness by other muscles. These isolated lesions must be recognized early. Early treatment for infantile paralysis in the orthopedic aspect consists in protection of the paralyzed muscles. This alone prevents deformity.

Saturday Morning, Oct. 17, 1931

EMOTIONAL REACTIONS IN EARLY CHILDHOOD AS CONDITIONING TREATMENT. ADA HART ARLITT, PH.D., Cincinnati.

There are two points which it would seem well to keep in mind in dealing with young children, both during the onset of illness and through its length and convalescence. The first is the extreme ease with which emotional states, particularly fears, are set up and transferred, and the second is the fact that the basis for many mental abnormalities is laid during the preschool period. Illness and convalescence provide a fertile soil for the development of atypical reactions.

In connection with the first of these points, the setting up of fear states, it is well to keep in mind the fact that though a few fear states are the result of direct experience, more appear to be set up by imitation and by verbal conditioning. Great as is the suggestibility of the average adult, that of the young child surpasses it. Speaking of the expected symptoms in the presence of the child sometimes sets them up, and often in a more marked degree than would seem possible. An illustration will serve to prove this point. We have had many children come in for reconditioning in regard to foods because they have been told while ill that these foods will make them sick. After the illness has disappeared and with it all necessity for refraining from this diet, nausea follows the eating of the once forbidden foods. If caution had been given in a somewhat different way, such for example as, "These are foods to eat now so that you

can get well and eat all of these other things that you like," the conditioning would be quite different.

Fears are transferred with extreme ease. In one case a child feared all white uniforms, even when worn by waitresses in restaurants, because during the time his head was being dressed after an operation on the mastoid, he had been told that the nurse would cut off his ears if he moved. Even more pathologic illustrations of transfer might be cited were there space for them.

Suppressed fears and anger states, types of withdrawal and the escape and defense mechanisms, may all be seen in the behavior of young children and may at that time be conditioned in such a way as to prevent or to make less likely the development of pathologic trends.

TUMORS OF THE BRAIN IN CHILDREN. DR. B. N. CARTER, Cincinnati.

In a series of 817 cases of tumors of the brain from the Johns Hopkins Hospital, including Dr. Cushing's Series up to 1912 and Dr. Heuer and Dr. Dandy's series from 1912 until 1922, 15 per cent occurred in children under 12 years of age. Forty-six per cent of the tumors in children occurred in the cerebellum, 43 per cent in the brain stem, 8 per cent in the cerebrum and 5 per cent in the hypophysis. Solid gliomas and gliomatous cysts made up 54 per cent of the tumors; in 30 per cent of the cases, cysts were found.

The diagnosis of tumor of the brain in children is made by the usual signs and symptoms of increased intracranial pressure plus localizing signs. The intelligent use of the ophthalmoscope is essential to the diagnosis. Most value in localization is obtained by ventriculograms, the air being introduced either through the spine or through trephine openings in the skull.

The treatment for tumors of the brain is operative or operative plus deep roentgen radiation. The use of deep roentgen therapy has been increasing in recent years.

A study of the end-results in the series of cases mentioned shows the following:

Verified Cerebral Tumors: In the 21 cases of this type, the following results were noted: died soon after operation (within one month), 11; lived in comfort for from six months to one year, then died of disease, 3; lived in comfort for from two to six years, then died (1 of appendicitis), 3; living at the present time (1, four months; 1, five years), 2; not heard from, 2.

Verified Tumors of the Brain Stem: In the 16 cases of this type, the results were as follows: died soon after operation (within one month), 11; lived for from four months to one year, then died of disease, 3; lived for two years, then died of disease, 1; not heard from, 1.

Verified Cerebellar Tumors: The results in the 40 cases of cerebellar tumor were as follows: died soon after operation (within one month), 14; lived for from six months to one year, then died of disease, 8; well for from three to nine years then died, some of disease; others of unrelated conditions, 5; living and well at present, 10 (2 living and well one year, 4 living and well from two to four years, 3 living and well from four to six years, 1 living and well ten years); not heard from, 3.

THE SO-CALLED NEURAL RETICULUM OF THE MELANOMAS. DR. N. CHANDLER FOOT, Cincinnati.

Up to five years ago it was generally understood that the so-called melanosarcomas were tumors of the skin; that is to say, that they originated either in the pigmented cells of the epithelium or in the pigmented cells of the underlying connective tissue or derma. That divided the general theories on the subject into two headings, one concerning the epithelium and the other concerning the connective tissue.

It was not suspected that these tumors had anything to do with the nervous system until 1926, when Mascon, a French pathologist, demonstrated that the tumors had a close connection with the nervous system. This had been demonstrated in 1899 by Soldon, who wrote a rather suggestive article, but did not follow it through very well, so his article was refuted and not accepted.

Mascon showed in his work that the tumors of the type to which I refer, the pigmented moles, showed cells that were similar to the cells of the tactile corpuscles of Meissner. He also showed that the tumors regularly followed the dermal distribution of the sensory nerves and their fibers. He further demonstrated that the tumors were closely associated with large groups of fibers by his trichrome method. He tested out, rather incompletely, the silver impregnation of these tumors in order to see if he could demonstrate the nerve fibers by the methods that were followed by Cal. He said that he left the work to people who were more used to the silver methods than himself.

I do not intend to qualify as an expert in silver methods, but I do know more about them, perhaps, than I know about anything else, so I thought it was a good chance to check up on Mascon. Mascon indicated in his paper that he thinks that the fibers in connection with these tumors are nerve fibers; that is, dermal fibers of the sensory nerves. I cannot tell definitely whether they are or are not, but I can show some suggestive things about them.

Mascon put a great deal of weight on the fact that the pigmented cell is not the only one concerned with a melanoma. Although it is spoken of as a pigmented tumor, the pigmented cell is merely another phase of the tumor cell in which pigment metabolism plays the chief rôle.

GLANDULAR DYSTROPHIES AND CONDUCT DISORDERS OF CHILDREN. DR. LOUIS A. LURIE.

The endocrine glands are the dominant factors in determining bodily structure.

Physicians should bear in mind that the correlation between structure and function long noted by physiologists includes both mental and physiologic functioning.

Disturbances in glandular function may lead to abnormal conduct reactions either directly or indirectly; directly, as in cretinism, in which the lack of thyroid secretion is responsible for the mental retardation; indirectly, as in cases in which as a result of physical malformation, such as midgets and giants, the patient develops abnormal mental attitudes and personality traits which make normal social adjustments difficult if not entirely impossible.

The close relationship existing between endocrine disturbances and delinquency, incorrigibility, sexual perversion, crime and other antisocial states has been demonstrated in a sufficient number of cases at The Psychopathic Institute of the Jewish Hospital (10 per cent in a series of 500 cases) to warrant the statement that no study of a child who presents a behavior difficulty is complete without a thorough study of the glands of internal secretion.

A number of cases showing such correlation were demonstrated.

LEAD STUDIES ON CHILDREN. DR. ROBERT A. KEHOE, Cincinnati.

Observations on the excretion of lead of thirty-seven infants and small children, carried out as a part of a search for the origin of "normal" lead as seen in the general adult population, have served to show that children, even exclusively breast-fed children, excrete small quantities of lead in both urine and feces.

The data presented show that children are born with lead in their tissues, and that even their mother's milk contains small amounts.

Lead is excreted more readily than was previously believed, and, when absorbed in small quantities, it accumulates to a much smaller extent than has been thought.

These findings are discussed in relation to the already difficult problem of the diagnosis of lead poisoning in children. Case examples were used to show that adequate quantitative analytic data are of the utmost value in this connection.

LABORATORY AND CLINICAL ASPECTS OF JAUNDICE. DR. LEON SCHIFF, Cincinnati.

Estimations of the serum bilirubin in more than 200 normal subjects revealed values of 0.6 per hundred cubic centimeters or less in more than 95 per cent.

In new-born infants, a concentration of over 1 mg. was frequently encountered. In children, the values were essentially those of adults. The levels were higher in males than in females and frequently seemed to bear a direct relationship to the hemoglobin and red cell content.

The ominous significance of jaundice — latent as well as clinical — in congestive heart failure was emphasized. Icterus was most frequently encountered in cases of rheumatic heart disease with mitral stenosis. Both the hemolytic and the obstructive types were encountered, and a possible explanation of the mechanism was given.

Instances of a decrease in jaundice in the presence of complete obstruction were cited.

Jaundice in lobar pneumonia was most frequently seen in right-sided lesions. It was found to be of bad prognostic significance.

Observations were also reported in cases of catarrhal jaundice, splenomegalic hemolytic icterus, sickle cell anemia, postarsphenamine hepatitis and a number of other conditions.

SPECIAL CASE REPORTS

ALBINISM. DR. KARL G. ZWICK, Cincinnati.

Through the courtesy of Dr. Graeme Mitchell I am granted the opportunity to present two brothers, L. A. (aged 14) and L. R. (aged 13), who are patients at the Childrens' Hospital Clinic.

The joint record of the essential clinical data is briefly as follows: The patients have had defective vision since birth; they are in the sight-saving class. They have continuous headache in the frontal region and at times nausea.

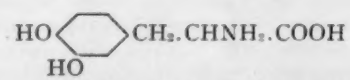
The past history is irrelevant; the patients have had no contagious diseases. The father died of pulmonary tuberculosis. The mother is in good health; one brother has defective vision.

Physical examination showed the skin and hair to be very white. There are nystagmus and photophobia. The cornea lacks pigment.

The diagnosis is albinism.

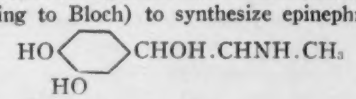
The patients merit interest because they afford an opportunity to study one phase of melanin formation in the skin and put to the test, as it were, Bloch's conception of melanogenesis. Briefly stated, Bloch's investigation of melanin formation originated from the following considerations: (1) in melanocarcinosis with melanuria, involving excessive pigment formation, the urine contains excessive amounts of catechol derivatives; (2) in Addison's disease, with dysfunction of the suprarenals, there occurs a bronzing of the skin. The first fact indicates the close connection between the melanin precursor and the orthodihydroxy benzene. The second fact suggests a relationship between the propigment (= precursor = chromogen) and epinephrine, which in turn makes it probable that the melanin is derived from a chromogen related to a tyrosine derivative having two hydroxyl groups attached to adjacent carbon atoms in the benzene ring.

The chemical compound that Bloch believes to be the precursor of melanin is 3, 4 dioxyphenylalanine:



According to Bloch's theory, melanogenesis (melanin formation) in the skin consists essentially in the conversion of the chromogen (= propigment = melanogen): 3, 4 dioxyphenylalanine into melanin by the action of a specific enzyme (= oxidase).

In hyperpigmentation of the skin in Addison's and related diseases, the impaired suprarenal glands fail (according to Bloch) to synthesize epinephrine:



from its mother substance, 3, 4 dioxyphenylalanine, which is therefore present to excess in the blood. When the excess reaches the skin, it is converted into melanin by the specific oxidase, and hyperpigmentation results. The pigmentation may be characterized as an excretory function.

The albinism, or an absence of cutaneous pigment, that exists in the two patients presented may be due to the absence of: (1) 3, 4 dioxyphenylalanine (melanogen), (2) the specific oxidase or (3) both factors.

According to von Grör, we can test for the presence of oxidase by the local application of 3, 4 dioxyphenylalanine to the superficially abraded skin. A demonstration of von Grör's test showed: (1) no melanin formation in the albino, and (2) melanin formation in a normal person. The result of von Grör's test supports Bloch's theory of the chemical mechanism of cutaneous melanogenesis with reference to the presence of the oxidase.

So far we have no simple means of determining the presence of the chromogen.

HEREDITARY ECTODERMAL DYSPLASIA: ANHIDROTIC TYPE. DR. MENDEL ZELIGS, Cincinnati.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

SUBLINGUAL GROWTH: RIGA'S OR FEDE'S DISEASE. DR. D. J. BRADLEY, Cincinati.

In November, 1930, a girl, aged 8 months, was brought to my office on account of a tumor under the tongue. This tumor had been present for about two months. The parents were native born. Three older children were alive and well. There was no family history of tuberculosis or syphilis. The general health of the baby was excellent. She was entirely breast fed, except for cereals, which she had difficulty in swallowing. It was this difficulty that called the parents' attention to the growth.

Physical examination gave negative results except for the findings in the mouth. There was no enlargement of the lymph glands of any region. The growth was first noticed shortly after the lower central incisors appeared. They were the only teeth present, and their cutting edge was rough.

The tumor had bled at times at the onset. It was wedged between the tongue and the floor of the mouth and was attached to the frenulum. It was a pearly gray, disklike body about 1.5 cm. in diameter and 0.25 cm. thick. In size and shape it resembled a candy "Life-Saver." It was hard, and its surface was rough. The depressed center showed some sloughing. The growth was movable and was attached to the frenulum by a wide base.

The Wassermann and tuberculin tests gave negative results. A culture taken from the surface of the tumor was negative for Vincent's angina and diphtheria organisms.

The growth was removed on Nov. 20, 1930, at the Good Samaritan Hospital, by Dr. Louis Feid of the surgical staff.

The laboratory report given by Dr. J. Ganim, the pathologist, is as follows: The specimen consists of a roughly circular pad of rather firm, gray tissue, averaging 0.75 cm. in diameter and 0.25 cm. in depth. The center is transversed by a horizontally directed cleft.

Microscopic examination of the tissue of the mucous membrane was made. The diagnosis was epithelial hyperplasia. The underlying stroma consisted of rather dense fibrous tissue. This was classified as a papilloma. At the present time, ten months after the growth was removed, the child is well and there has been no recurrence of the disease.

The sublingual growth I have just described occurs most frequently in southern Italy. Different Italian authors have reported as many as 400 cases of the disease. This accounts for its many different names — Riga's disease, Fede's disease, etc.

Its rarity in this country is the reason for presenting this case. The first report of a case of this condition in the United States was in 1903, by Dr. Samuel Amberg of Johns Hopkins University.

Italian authors regard the tumor as a product of inflammatory processes. The stretching forth of the tongue over the lower incisors causes a slight abrasion on the frenulum. In this place, denuded of its epithelium, parasites are deposited; either the usual inhabitants of the mouth or others. Here the parasites may complete their evolution, causing a local reaction, in which the hyperplasia of connective tissue predominates. The result is a fibroma or a papilloma.

CONGENITAL ANOMALY. DR. GEORGE F. PATTERSON, Cincinnati.

G. A., a girl, who was born on Nov. 29, 1928, was admitted to the hospital on Feb. 4, 1931. The present illness began at 2 months of age. At that time she had an acute respiratory infection following which the urine assumed a milky color. An analysis showed it to be loaded with pus. Since that time, in spite of treatment, the urine has retained this characteristic.

The symptoms consist of frequent and difficult urination. Within the last three weeks there have also been dysuria with associated enuresis, and abdominal pain, anorexia and intermittent periods of fever.

The patient was born following eight months of pregnancy. The birth weight was 5½ pounds (2,494.7 Gm.); delivery was normal. She was breast fed for six months. She sat up at 5 months, and walked at 16 months.

The family history is unimportant except for the fact that the maternal grandfather died of tuberculosis.

Physical examination revealed a small, anemic child, weighing 20 pounds and 5 ounces (9,213.5 Gm.). She was very active. There were no palpable masses in the abdomen.

She has rudimentary metacarpals on the left thumb. The second and third toes on the left foot are webbed.

Examination of the blood showed: red cells, 3,500,000; white cells, 10,500; hemoglobin, 70 per cent, with a normal differential count. The phenolsulphonphthalein excreted in the first hour was 45 per cent; in the second hour, 15 per cent, a total of 60 per cent. The urine was loaded with pus cells and showed 1 plus albumin.

On February 26, 10 Gm. of iopax was injected intravenously. The following report was made: Roentgen examination of the genito-urinary tract made following the injection of iopax by Dr. Harris shows no outline of the kidney, pelvis or ureters. This may be due in part to a large accumulation of gas and some fecal matter scattered through the abdominal cavity. The urinary bladder is definitely outlined by the accumulation of the iopax.

On February 9, a cystoscopic examination was made by Dr. B. O. Swarz. The bladder showed no pathologic changes except an absence of the left ureteral orifice and marked inflammation around the right ureteral opening, near the midline.

The right ureter was catheterized, and a pyelogram was made following the injection of 10 cc. of skiodan solution.

The roentgen report was as follows: Examination of the genito-urinary tract following the injection of the ureteral catheter into the pelvis of the right kidney showed no evidence of stone. Following the injection of 10 cc. of skiodan through the ureteral cavity by Dr. Swarz, a bifid type of pelvis with moderately enlarged calices was seen in the lower pole. There was a slight enlargement of the outline of the kidney.

A later catheterization was done, and the pelvis was washed out with 4 cc. of a 1 per cent silver nitrate solution. The patient reacted normally, and since that time she has gained about 4 pounds (1,814.3 Gm.), and has had less abdominal pain; urinalysis gives much improved results, and the (anorexia) has disappeared.

ANTRUM LAVAGE. DR. S. K. SIEBLER, Cincinnati.

A. L., a girl, aged 3 years, was admitted to the Jewish Hospital on Oct. 18, 1930, with the chief complaint of pain in abdomen and fever. For the past six weeks, she had been having frequent attacks of sharp pains in the abdomen, intermittent attacks of fever and loss of weight. She had been listless during these attacks and refused any kind of food. There was no history of vomiting, diarrhea or constipation. The attacks came on without any reference to the taking of food.

Three days before admission to the hospital, a serous nasal discharge, without a cough, developed.

The past history was essentially unimportant. The positive physical findings on examination consisted of a markedly dry skin with inelasticity, showing loss of weight. Both tonsils were injected; the left was larger than the right. There was a marked postnasal drip. The cervical glands were slightly enlarged. The breath sounds were somewhat diminished over the left base posteriorly.

Following admission many urinalyses were made, some of which showed clear fluid, while others showed large numbers of pus cells. The red cell count varied from 3,800,000 to 4,300,000. The leukocytes varied from 13,700 to 28,000; the polymorphonuclears, from 75 to 83 per cent.

The temperature ranged from 99 to 104 F., being both intermittent and remittent. X-ray pictures showed a marked cloudiness over both maxillary sinuses. Pictures of the chest and abdomen were negative.

On entry the child weighed 23 pounds and 2 ounces (10,489.5 Gm.), the weight being 22 pounds and 7 ounces (10,177.6 Gm.) after she had been in the hospital about a week.

On October 20, bilateral otitis media developed, and in spite of the fact that the condition cleared up, the temperature continued septic in type. The child's condition became much worse, and on October 30, her condition was so bad that we felt that something had to be done at once.

Consultation with the genito-urinary specialist was asked for, and the advice was to do a pelvic lavage of the kidneys. Before carrying out this procedure we decided first to lavage the antrums, and this was done on October 30. The antrum washings revealed a foul-smelling, sanguineous pus, containing chiefly staphylococci. Several hours after the washing the temperature dropped to normal and there was a remarkable improvement in the child's general condition. Shortly afterward she developed a marked appetite. The urine became clear, and the weight gradually increased. At the time of discharge, she weighed 25 pounds and 4 ounces (11,453.4 Gm.), a gain of almost 3 pounds (1,360.7 Gm.) of her lost weight.

The tonsils were removed several weeks after the lavage of the antrums and the child made an uneventful recovery.

This case was presented to show that occasionally lavage of the antrums is of marked benefit and, as in this case, is the basis of infection in other parts of the body; the symptoms and the physical signs immediately cleared up when care was taken of the sinuses.

CONGENITAL ANOMALIES OF THE EXTREMITIES. DR. LEO FRIEDMAN, Cincinnati.

Children who present deformities of the extremities are of interest not only from the standpoint of anatomic anomalies, but also from the point of view of interference with function and the relation of the latter to the future life of the patient. Corrective procedures, if at all possible, are, of course, dependent on the degree of deformity.

L. K., a boy, aged 13, first came under observation at the Jewish Hospital, having been referred for study to the Psychopathic Institute of the hospital by the Juvenile Court. He had used his deformity to excite pity while begging on the streets.

The history was not important except that the deformity had been present from birth. The family history was irrelevant. Physical examination revealed a well developed boy, of 13, who displayed an anomaly of both arms, otherwise, the results were essentially negative.

Both arms were shortened and were held partially flexed with the elbows appearing very prominent. Neither arm could be fully extended. The left forearm could be flexed normally, but the right arm was maintained at an angle of 120 degrees. The right ulna was missing, and there were but three fingers on each hand, apparently corresponding to the thumb and the middle and little fingers in each case.

The boy is able to handle himself very well; he shows great skill in shuffling cards, buttoning clothes and all such fine manipulations. Apparently he suffers from no material handicap as a result of his deformity.

R. R., a girl, aged 11, was first seen during routine physical examinations of a number of children. It was noted that she was extremely short for her age, and this fact led to further study.

She was born at full term; the delivery was normal. Aside from her physical deformity, she appeared to be in good condition at birth. She had always been in good health and appeared to develop normally except for the fact that she began walking rather late. There was no familial history associated with any deformity.

Physical examination revealed a white girl of 11 years who appeared much smaller than her age suggested. She was 39 inches (98.5 cm.) tall, weight 57 pounds (25,855 Gm.) and was well nourished. Except for her local condition, she appeared to be quite normal. The lower extremities were both very short, and there was no joint corresponding to that of the knee. Apparently a single bone extended from the hip to the foot on either side. The thighs were well developed, and from the hips downward there was a rapid decrease in the circumference of the extremities. There was a marked pronation of both feet, the latter showing in addition congenital deformity as characterized by the presence of four toes on the left foot and three on the right. The gait was of the waddling variety with the legs held stiff, the femur articulating directly with the os calcis.

Although this little girl is considerably smaller than the companions of her own age, reaching a short distance above their waists, she is very active and is able to hold her own in the usual children's games. She is very cheerful and takes part in all the pastimes, such as jump the rope, play ball, etc. She is able to get up and down stairs with remarkable speed.

STUDY OF A CRETIN. DR. ALICE F. LYLE, Cincinnati.

The patient, aged 7 years, was a typical cretin. The basal metabolic rate was 140. The skin was pale and wrinkled; the hair was coarse; there was macroglossia, and the abdomen was prominent. These findings illustrate physical retardation. The mental age was 3 years; the intelligence quotient, 40. Under treatment the patient has improved along physiologic lines. Cretins and patients with congenital syphilis, if neglected, increase the inmates of public institutions.

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Nov. 17, 1931

JESSE R. GERSTLEY, M.D., *Presiding*

PAROXYSMAL SNEEZING IN WHOOPING COUGH. DR. ALWIN C. RAMBAR.

A girl, aged 23 months, was brought into the graduate premature clinic with the complaint of having had a "cold in the head" for two weeks. During the

past week she had been sneezing forcibly and frequently. Following a period of crying, she had an attack of sneezing, which I witnessed; it consisted of a series of from eight to ten paroxysmal explosive sneezes. At the end of the attack the child became cyanotic, and with the last sneeze expelled a large quantity of thick mucopus from both nostrils. Following the attack she was exhausted. The white cell count was 19,000; the differential count showed 72 per cent small lymphocytes. These attacks occurred from ten to fifteen times in twenty-four hours and persisted for three weeks. At this time the sneezing changed to the characteristic cough and whoop of pertussis. A diagnosis of pertussis was made from the paroxysmal quality of the sneeze, with the resulting cyanosis and expulsion of mucopus from the nose, which so closely resembled the usual paroxysms of coughing in pertussis.

Though as early as 1813, Watt mentioned the occurrence of pertussis with coryzal symptoms alone, reports of only a few such cases appear in the literature.

Empyema Necessitans. Dr. A. Matheson.

I wish to present a case of empyema necessitans in an infant 10½ months old. She was admitted to the hospital on Sept. 23, 1931, because of a swelling below the left scapula of ten days' duration.

Labor and birth were normal. The child was breast fed for four months. Cod liver oil was given. At 5 months a severe eczema appeared on the face and arms, and there was secondary cellulitis of the right arm. In July, the mother noted a discharge of pus from both ears accompanying pharyngitis. No medical aid was sought. In the interval between this illness and the time of admittance to the hospital, no history of an acute infection was obtainable. The mother said that she had believed the infant to be well, except for failure to gain weight, and profuse sweats. Ten days before admittance to the hospital swelling appeared below the left scapula. A physician wanted to incise the abscess, but the parents objected. On September 23, another physician was called because marked dyspnea and cyanosis suddenly developed, and because the swelling seemed larger. The infant was hospitalized; the abscess incised, and about 1½ pints of pus was obtained. In making the incision the surgeon noted marked separation of muscles and rupture of muscle fibers. He suspected a cold abscess secondary to tuberculosis of the spine. A roentgenogram revealed empyema of the chest on the left side. The closed method of draining was used. Subsequent films of the chest were taken to show progress. In ten days the infant left the hospital free from symptoms or signs of thoracic disease. At the time of presentation she is in excellent physical condition.

On admission the white blood cells numbered 26,000. A culture of pus taken following thoracentesis showed Streptococcus haemolyticus. A culture of pus from the incision of the subcutaneous abscess showed Streptococcus haemolyticus. Tests with tuberculin gave negative results. The urine was normal.

Empyema necessitans usually results from neglected empyema of long duration. Rupture through the wall of the chest usually takes place in the parasternal line, since the wall is thinnest at that location.

Ocular Torticollis. Dr. M. A. Perlstein.

Ocular torticollis is a condition in which turning and tilting of the head to one side occur to compensate for lack of binocular vision.

Turning of the head to the right or left side occurs in lateral diplopia; tilting up or down occurs in vertical diplopia, and inclining to one or the other shoulder occurs in oblique diplopia. Therefore, it should be possible to infer from the position of the head which muscle is responsible for the ocular defect.

When the child presented was 6 months old (she is 3 years old now) her parents noticed that her eyes were crossed, and that she turned her head to one side when trying to focus on any object. This condition has persisted, and it is more evident when the child is playing outdoors than when she is in the house.

As you see, she holds her face turned to the left, her head being inclined toward the left shoulder and tilted up, i. e., with her nose in the air. Frequently, however, when she tries to focus with the right eye, she turns her face to the right and tilts her head in the same direction.

Examination of the eyes was made by Dr. Gradle, who reported that there is a convergent strabismus of 35 degrees and a supervergent strabismus of 3½ degrees of the right eye; that is, the right eye turns in and up, indicating a weakness of the right external rectus and of the right superior oblique muscles. In addition there is moderate hyperopia and astigmatism. Since the right externus pulls the right eye to the right, and since the right superior oblique pulls the eye down and out while rotating it inward, the various positions assumed by the child's head may be explained by weakness of the several muscles combined.

Ocular torticollis is not to be confused with muscular wryneck. In muscular torticollis there is an actual hardness or spasm of the muscle. Moreover, the patient is unable to move the head in all directions at will.

The treatment for ocular torticollis consists in treatment for the condition of the eyes, which in this child would be the use of glasses to correct the astigmatism and hyperopia, orthoptic exercises to strengthen the optic muscles, and finally tenotomy of the opposing muscle in the same eye or of the same muscle in the opposite eye, so that both eyes will move in unison.

HYPOTHYROIDISM WITH COMPLICATING DUODENAL ULCER. DR. JULIUS H. HESS.

This girl is 11 years of age. At 2 years of age she had pneumonia complicated by empyema; she had nasal diphtheria in 1925 and measles in 1926; she has also had pertussis and chickenpox. In 1930, she had a suppurative cervical adenitis. Her tonsils and adenoids were removed in 1928. Her appetite was always poor and capricious.

The father stated that nothing abnormal was noted in her mental state or physical development until 3 years ago, when her skin became rough; she lost most of her hair, which had been of fine texture, and the new hair was dry, coarse and very sparse, and she seemed to stop growing.

On admission to the hospital she weighed 59 pounds (26,800 Gm.); the normal weight for a child of her age would be 63 pounds (28,600 Gm.). During the three days' observation before thyroid was given, the patient lost 9 pounds (4,082.33 Gm.), in all probability owing to lack of food intake and brooding. The standing height was 49 inches (124 cm.); the normal height for her age is 52.2 inches (132 cm.). The sitting height was 24.45 inches (62.9 cm.) as against the normal height of 28 inches (71.1 cm.). The shortness of the body is in the trunk rather than in the lower extremities. She has the typical hand of a patient with hypothyroidism.

About one and a half years before presentation she lost all interest in outside activities, and it was with difficulty that her mother could persuade her to play with other children. She complained repeatedly to her parents of being cold and liked to be near the radiator. She had not been seen to sweat during the past three years. At the present time, at the age of 11, she is in the seventh grade, and is said to be carrying her school work to good advantage. This is exceptional for a child showing deficient thyroid secretion.

About six years prior to presentation she started to complain of pain in the epigastric and left hypochondriac regions. She states that these pains were stab-like and occurred irregularly, and that they were more or less continuous up to the time when she was admitted to the hospital. Repeated roentgenograms of the gastro-intestinal tract showed a duodenal defect. Examinations of the stools have all given negative results for blood. It is my impression that this child has a healing or healed duodenal ulcer.

The first determination of the basal metabolic rate gave a result of —40; the second one, taken before thyroid was given, —49; and one taken eleven days after

the thyroid was given, —15. After being under treatment for twelve days, the general appearance had changed materially. She was more alert and happier. She did light work about the ward. I think that the change has been sufficiently striking to be noticeable to all those who have come in contact with her. She has changed in disposition. When she first came into the hospital she was morose; now she is happy.

While in the hospital the patient received 5 grains (0.324 Gm.) of thyroid gland daily. After she was discharged from the hospital, the family complained of her restlessness and talkativeness. The administration of thyroid was then cut down to 4 grains (0.26 Gm.) daily. At this time she weighed 51½ pounds (23.3 Kg.); she had lost most of her dry hair, the texture of her skin had greatly improved, the pulse rate was 126, she rarely felt cold, and she was still decidedly restless.

The basal metabolic rate is now plus 12. The dose of thyroid has been gradually reduced to 1½ grains (0.097 Gm.) daily; in addition, the patient receives 1 drop of compound tincture of iodine daily. She is also receiving 4 cc. of a liver and iron compound daily. Since she was first seen the hemoglobin has increased from 58 to 68 per cent, and the blood picture shows general improvement.

She is back in school; she enjoys her activities and in every way acts and appears normal, except for her small stature.

Lavage with Mercurochrome-220 Soluble. Dr. A. Levinson.

In the last few years six cases of meningitis have been reported in which mercurochrome-220 soluble has been injected intrathecally. No therapeutic results were obtained in any of these cases, as all of the patients died, three of them during the time when the mercurochrome was being injected. One had a severe but not lethal reaction, and two showed no reaction immediately, but they all died of meningitis.

A patient came into the meningitis service of the Sarah Morris Hospital suffering from a streptococcal meningitis following mastoidectomy. The child was moribund, and all treatment had been of no avail. Lavage from the cistern to the lumbar region was employed, a 0.1 per cent solution of mercurochrome being used (instead of 1 per cent, as has been used in the cases reported); 90 cc. of a 0.1 per cent solution of mercurochrome was injected, and 70 cc. was removed, without apparent ill effects. However, the child died two hours later. At necropsy we found that the mercurochrome had discolored the ventricles and also the posterior part of the cortex. We checked the bactericidal action and found that the amount injected was not entirely bactericidal, as, after standing for one hour, streptococci were still found in the mercurochromized fluid. Dr. Perlstein and I tried to determine the effect of the intrathecal injection of mercurochrome in dogs, and we found that when lavage with a 0.1 per cent solution of mercurochrome was performed there were hemorrhage and necrosis in the white matter all the way from the brain to the lumbar region. This has convinced us that mercurochrome is dangerous for intrathecal treatment. We have not given up the idea of intrathecal lavage in meningitis, however, but are trying to find a chemical that is bactericidal in subtoxic doses.

Pityriasis Rubra Pilaris. Dr. E. P. Zeisler.

Dr. Gerstley has asked me to present this case. All of you who have had the opportunity of seeing it will agree that it is very unusual. This child is 7 years old. She was well until two weeks before presentation. The condition began around the mouth as a patch of redness and numerous papules which coalesced and gradually spread until in two weeks the entire body had become involved. The child was never sick before and had never had a similar condition. No one else in the family has had any condition like it. One's first impression is that the child has an exfoliative dermatitis. The skin is uniformly red. The scalp is very scaly. The face is red and diffusely scaly. One can notice a slight beginning ectropion around the eyelids. The body shows diffuse inflammation with areas of

normal skin here and there. On close examination, however, these patches of apparently scaling dermatitis are composed of fine discrete conical papules, and on palpation there is a feeling like a nutmeg-grater. The lesions are located around the hair follicles, and only here and there do they coalesce to form these scaling patches. Over the knee are scaling patches that look like those seen in psoriasis. The palms and soles show hyperkeratosis. No laboratory examinations have been made as yet. The impression that the intern received was that the child had a scaling erythrodermia, a toxic erythema, a toxic dermatitis or acute psoriasis.

All four diagnoses are incorrect. The condition is a classic example of the extremely rare and unusual disease of the skin called pityriasis rubra pilaris, or Devergie's disease, and it is identical with the condition described many years ago by Kaposi as lichen ruber acuminatus. It is an inflammatory disease of the hair follicles of unknown etiology. None of us has seen many cases. I have seen perhaps ten or twelve. The condition begins in early life, occasionally with an acute onset, as in this case; at one stage it may develop into an almost universal exfoliative process, and then gradually recede and leave a residual chronic inflammation. The only typical finding that is lacking is the presence of horny plugs on the dorsal phalanges. Most of the cases that I have seen have been chronic, and improvement has been gradual. Some French authors think that there is an underlying tuberculosis; others think that there is an underlying endocrine disturbance, and have noted improvement on the administration of thyroid. The treatment is empiric, as in acute psoriasis, consisting of mild local applications and colloid baths. I present this case, therefore, as a rare case of pityriasis rubra pilaris of generalized type. A patient with this disorder was under the care of my father about thirty years ago, and the question of marriage came up. He was advised that it was perfectly safe for him to marry, as the disease had never been known to be hereditary. Four children were born, in three of whom this condition developed early in life; all were treated by us.

CASE OF MULTILOCULAR CYSTIC HYGROMA. DR. I. RUBELL.

An infant, 6 weeks old, was brought into the clinic one week prior to presentation with a history of having had a swelling of the left side of the neck which the mother had noticed two weeks previously. There were dyspnea and difficulty in swallowing and a gurgling sound in the throat when the baby took the bottle. Occasionally there was cyanosis accompanying the feeding. On examination there was a soft, globular mass between the midline and the border of the sternocleidomastoid muscle. The impression was that the condition was a bronchial cyst, or a cystic hygroma as a second possibility. Because of the possibility that a cyst was present, we looked for a fistula, because frequently such cysts have fistulous openings into the pharynx. Examination revealed no such opening. It then occurred to us that we might be able to visualize this by reaching the mass from the outside and putting in some radio-opaque substance for roentgen examination. With a needle 17 cc. of a viscid material was obtained which on examination showed a few epithelial cells. Chemical examination showed 250 cc. of cholesterol per hundred cubic centimeters of fluid. The roentgenogram exposed at that time showed nothing in the neck but a small circular shadow in the upper part of the substernal region. A needle was introduced a day later, and 25 cc. more of fluid was obtained. Iodized oil was injected through the same needle and another film exposed. This film showed a large cystic mass in the neck, which on being filled up showed clearly. With the possibility in mind that the condition was a bronchial cyst with a possible fistula, we waited twenty-four hours and then another film was exposed. This film showed that there was a tunnel leading from the mass downward and medially somewhere into the mediastinum. At that time the child became dyspneic and cyanotic and had a marked stridor. At that time it occurred to us that possibly this fistulous tract opened somewhere into the trachea. The symptoms became so pronounced that tracheotomy was decided on. As the surgeon cut into the neck, he incised another large cyst, and

a great deal of material escaped. Dr. Strauss suggested that the appearance of the fluid was identical with the fluid previously obtained from the mass in the neck. This would make the diagnosis of cystic hygroma positive. The original cyst was probably a substernal cyst, and when the iodine was injected it gradually forced its way through the fistulous tract into the substernal cyst, which became distended and produced the marked dyspnea. As soon as the fluid escaped, the child began to breathe freely, and a tracheotomy became unnecessary.

The treatment for cystic hygroma is unsatisfactory. The surgical treatment is impracticable. Two cysts have already been demonstrated. Many others may be present, so that surgical removal will be impossible. The injection of iodine has been suggested with the idea of producing an inflammatory reaction and obliteration with scar tissue. At present, the use of roentgen rays and radium seem to be the treatments of choice. So far as I can find in the literature, this is the first attempt to fill such cysts with iodized poppy seed oil (40 per cent) and to visualize them roentgenographically.

INTERESTING ALLERGIC PHENOMENA: URTICARIAL PIRQUET REACTION. DR. I. HARRISON TUMPEER.

Eleven months prior to presentation, this 5 year old girl passed a systematic physical examination. The reaction to the Pirquet test was negative and a fluoroscopic examination of the chest showed it to be normal. Four weeks previously, a high, sustained fever developed, which persisted until one week prior to presentation. There were no physical symptoms, except pallor and a tired appearance, and the child made no specific complaints. The white cell count was 3,000, and the typhoid agglutinations were negative. An unusually extensive reaction to the Pirquet test occurred, taking the form of an urticarial response with marked pseudopod formation. Fluoroscopy revealed enlarged mediastinal glands. It seems that in this case we happened to strike the stage of the development of allergy in the tuberculous invasion.

TRANSFER OF HORSE SERUM SENSITIVITY FROM A CASE OF ARTHUS PHENOMENON. DR. I. HARRISON TUMPEER.

This 5 year old girl is the second patient with Arthus' phenomenon we have had this year. At a previous meeting of the society, I demonstrated a marked case which had progressed to the stage of sloughing, leaving the muscles exposed as in an anatomic dissection. Fortunately, in this case, the process stopped at the stage of marked induration, swelling and pallor of the inoculated area. The steps in the evolution of this lesion were as follows: The patient had received the usual three weekly inoculations of horse serum toxin-antitoxin four years previously. Three months before presentation she was given tetanus antitoxin for a lacerated wound. One month before presentation she again received tetanus antitoxin for a similar lesion, following which the typical progression of the Arthus reaction occurred, including such details as the involvement of parts distant from the site of inoculation.

To determine whether the serum in such cases contains substances reacting with horse serum, the common denominator of the previous injections, passive transfer was performed, employing the mother as recipient. One-tenth cubic centimeter of the child's serum was inoculated intracutaneously into the mother's arm. In two days, 0.1 cc. of a dilution of horse serum was injected into this site and into an untreated control site. Within a few minutes there was a marked response at the site of the previous injection, the locally sensitized site, while the control site, representing the mother's native reactivity to horse serum, remained unchanged. This demonstrates that a specifically reacting antibody is present in the serum of persons in whom the hypersensitive state of the Arthus phenomenon develops.

UNUSUAL COMPLICATIONS OF PNEUMONIA IN INFANTS AND CHILDREN. DR. SOL LONDE.

CASE 1.—L. W., a girl, aged 9, was admitted to the hospital on Feb. 14, 1931, with the following complaints: cough for fifteen days, headaches, fever and pain in the right side of the chest for ten days, and the passage of blood in the stools and urine for the last thirty-six hours. There was no past history of any tendency to bleed.

On admission to the hospital, the temperature was 101 F. The pulse was rapid and thready, and the respiratory rate was 32. There were all the signs of a severe hemorrhage: marked pallor, perspiration, restlessness and extreme thirst. The systolic pressure was 70 and the diastolic could not be read. There were no purpuric spots. The breathing was rapid and shallow, and there were dulness, bronchial breathing and râles over the base of the right lung posteriorly.

The patient soon passed a stool consisting entirely of large clots of blood. The urine was loaded with red blood cells. The red cell count was 1,830,000; the hemoglobin, 50 per cent and the white cell count, 48,400, with 85 per cent polymorphonuclears, 12 per cent lymphocytes and 3 per cent monocytes.

The diagnosis on admission was confluent bronchopneumonia of the lower lobe of the right lung, possible septicemia and hemorrhage from the bowel.

The patient's condition was so grave that she was quickly given a transfusion of 300 cc. of whole blood. There was little improvement for the next forty hours; she continued to pass blood in the stools and urine. At the end of this time the patient was given a transfusion of 250 cc. of blood. The red cell count before the second transfusion was 1,730,000. The platelets numbered 120,000; the bleeding time was five minutes, and the coagulation time was three minutes.

Cultures of the blood gave negative results. Nidal and Shiga and Flexner dysentery agglutination tests were negative. Cultures of the stools revealed no specific organisms.

After the second transfusion the bleeding stopped, and the patient showed marked improvement. However, four days later pyopneumothorax developed. The pus, which was aspirated, yielded Staphylococcus haemolyticus and Pneumococcus type II. The right side of the chest was drained, and after a rather prolonged convalescence the patient was discharged, well, on May 15.

CASE 2.—R. R., a boy, aged 16 months, was admitted to the hospital, on Dec. 7, 1930. The complaints were cough, restlessness, fever and discharge from the ears for two days. The temperature was 102.4 F.; the pulse rate 160 and the respiratory rate, 34. Physical examination revealed an acutely ill, pale and flabby male infant. The respirations were rapid and grunting. There was a bilateral aural and a nasal discharge. The throat was red, and there was cervical glandular enlargement. The lungs were normal; there was a nontransmitted systolic murmur in the third interspace to the left of the sternum.

During the patient's stay in the hospital, the temperature was septic. Physical and roentgen indications of pneumonia in the upper lobe of the right lung developed within forty-eight hours after admission. On the morning of December 12, the temperature was 98 F., and the patient appeared as if he had gone through a crisis. However, in the evening the temperature again rose, and tense, tender purpuric swellings involving the left forefinger and middle finger appeared. Within the next few hours, the patient's condition became grave. Large ecchymotic swellings appeared, involving the left ear, the right side of the face, the forehead and the right hand.

The red cell count at this time was 3,570,000; the hemoglobin, 70 per cent. The platelet count was 140,000. The bleeding time was three minutes, but the blood did not clot. The patient was given a transfusion of blood, but he died within twenty-four hours after the appearance of the first purpuric spot.

Autopsy and cultures of the blood were not obtainable.

We were unable to find in the literature any reports of cases of purpura fulminans complicating pneumonia later than the reports and résumés of Nobécourt

and Mathien in 1920 and Bazan in 1921. In most of the cases mentioned the patients had pneumococcal septicemia. It may be of interest to mention that an in vitro product of the pneumococcus which when injected into rabbits causes purpura has been obtained.

CHLOROMA. DR. PHILIP ROSENBLUM.

A boy, aged 4½ years, was presented because of headache, pains in the arms and knees and discoloration of the lower eyelids, which had been present for two or three months. There were also slight fever, anorexia and loss in weight. Three weeks before entrance into the hospital, the tonsils and adenoids had been removed because of these symptoms, but there had been no improvement. The child entered the hospital on September 10, and died on November 22.

There were no characteristic observations on the blood, except those of secondary anemia. At no time was the white cell count more than 14,000. No embryonic cells were seen. The eyes and skull presented the most prominent changes. The discoloration and protrusion of the eyes increased until the left eye was completely destroyed. The left parietal bone became prominent and the sutures separated. There were also abnormal findings in the ribs, spine, extremities and lymph glands.

Roentgen therapy was tried, but no improvement followed.

Autopsy, which was performed by Dr. Otto Saphir, our pathologist, disclosed the typical changes of chloroma. Grossly, the involvement of the periosteal spaces of the bone of the skull, especially in the region of the orbit, the exophthalmos, the periosteal changes and the involvement of the peritoneal and retroperitoneal nodes were characteristic. Histologically, the type of cells resembling partly lymphocytes and partly myelocytes, their arrangement into rows and streaks, their invasive growth and the absence of basophilic granules were pathognomonic for the condition called chloroma. One important feature, however, namely, the green color that gives such growths their name, was not present in this case. But a number of cases are reported in all respects typical of chloroma, without the green color.

PAROXYSMAL HEMOGLOBINURIA. DR. JOSEPH K. CALVIN.

The patient, 2½ years old, has had three attacks of hemoglobinuria; the first one occurred when he was 20 months old, one three months ago and one two months ago. Each of these attacks was characteristic. They were ushered in by infection of the upper respiratory tract. When admitted to the hospital, the patient was almost exsanguinated. At that time, the hemolysis was so great that he had a moderate degree of jaundice, marked pallor and signs of shock. Each time he has been admitted we have resorted to intravenous transfusion. The mother's blood, which is compatible, causes a prompt response. Each of the three times the child has received two transfusions of the mother's blood, consisting of 200 cc., given five days apart. The child has come out of the state of shock and rapidly improved, so that within a few days the hemoglobinuria has disappeared. This condition has never lasted more than six days. During these attacks the child has marked secondary anemia; the red blood count averages between 1,500,000 and 2,000,000, and the hemoglobin between 30 and 40 per cent, and there are 30,000 leukocytes with from 60 to 70 per cent polymorphonuclears during each attack. The platelet count is normal. The blood urea is normal, and cultures of the blood are negative. The child has not had an attack for two months. The hemoglobin is now 70 per cent; the red cell count, 4,000,000, and the white cell count, 7,200. The urine is absolutely normal, with no red cells or hemoglobin at present. The child is well and never has been sick except for these attacks.

The most interesting factor is not so much the recurrence of hemoglobinuria as the etiologic factor. We made the so-called Langsteiner test to see whether this was a true paroxysmal hemoglobinuria; that is, artificial chilling of the

blood in a test tube caused marked hemolysis compared with controls. Of the cases reported so far, all have shown a positive Wassermann reaction. Syphilis seems to be the only etiologic factor. In this case, the Wassermann and Kahn reactions of the parents' and the child's blood were repeatedly negative. The child was also chilled by the immersion of his feet in ice cold water to see whether an artificial hemoglobinuria could be reproduced, as is done in the test tube in the Langsteiner test. It was impossible to do so. There was no history of purpura and no evidence of malaria, blood dyscrasia or rare tropical diseases that cause hemoglobinuria. The child shows a so-called paroxysmal hemoglobinuria which is activated by chilling but also seems to be precipitated by an infection of the upper respiratory tract. The first attack occurred in August, during a very warm period. The attempt to produce the attack artificially by chilling the patient was unsuccessful. The child has a so-called autohemolysin in the blood activated by chilling. This test has been repeated, each time with positive results. The tuberculin test is negative.

APLASTIC ANEMIA. DR. ETHEL M. DAVIS.

The patient has been in the hospital since early in June, 1931, when she entered with the complaint of pallor, apathy and a feeling of chilliness. Physical examination showed a child of 6, with marked pallor, moderately enlarged tonsils and small, palpable cervical lymph glands. The liver and spleen were palpable two fingerbreadths below the costal margin. Examination of the blood showed 2,900,000 red cells, 50 per cent polymorphonuclears, 86 per cent lymphocytes, 1 myelocyte and 0.25 per cent reticulocytes. The platelet count was normal. The temperature, always below 100 F., at the end of September suddenly rose to over 105 F., and the child became toxic and apathetic. Examination revealed a small necrotic area in the center of the right buccal mucosa. She was given 0.3 Gm. of sulpharsphenamine intravenously, and within twenty-four hours the temperature fell to approximately normal. At that time there was a leukopenia with 200 white cells and a differential count of 3 per cent polymorphonuclear leukocytes, 5 per cent monocytes and 92 per cent lymphocytes.

The question of diagnosis in this case is of interest. Because of the relatively high white cell count, from 2,000 to 5,000, the case apparently does not fall into the group of malignant leukopenias, in most of which the white cell count has been around 500 or less. Because of the absence of any early forms of blood cells on repeated examinations, the diagnosis of aplastic anemia has been considered. Except for one examination made five days prior to presentation, there has been no evidence of regeneration of the blood. On November 13, there were 5,000 white cells, 30 per cent of which were polymorphonuclears, which is the highest neutrophil count that has been present. At this time there were 62 per cent lymphocytes, 2 nucleated red cells and 30 per cent reticulocytes, indicating a definite activity of the bone marrow. Whether on this evidence one can still entertain a diagnosis of aplastic anemia is doubtful. The possibility of an aleukemic leukemia has been considered, but not more than one myelocyte has ever been seen in the smears. The child has received repeated transfusions of blood, intravenous and intramuscular injections of iron in various forms and treatment with violet rays and adenine. The recent report from Harvard Medical School on the treatment for persistent leukopenias with pentose nucleotides offers a method of treatment.

RAPID CURE OF AN INFANT WITH SECONDARY ANEMIA FOLLOWING ADMINISTRATION OF LIVER EXTRACT WITH IRON. DR. ARTHUR F. ABT.

A male infant born prematurely on July 25, 1929, after thirty-three weeks' gestation, weighing 1,690 Gm., was discharged from the premature station at the age of 5 weeks in an excellent physical condition, weighing 2,085 Gm. There had been no difficulty in nursing, and no cyanotic spells or abnormal symptoms were noted during the new-born period. The infant was taken regularly to the

outpatient department for examination and dietary instruction. At 3 months, egg yolk was added to the diet, and at 4 months, cereal feeding was started.

At 4½ months of age the infant weighed 5,500 Gm., and it was first noticed that he was extremely pale. At this time vegetable soup was added to the diet. At 6½ months of age he was still pale, and 1 grain (0.065 Gm.) of iron and ammonium citrate was administered daily. At 8 months of age more vegetables and fruits were added to the diet, and at 9 months the pallor was still marked and the infant had had a mild attack of rhinopharyngitis, with a low grade fever and slight diarrhea. Liver and beef juice were added to the diet, and the iron and ammonium citrate were increased to 1½ grains (0.097 Gm.) daily. At 10 months of age, the patient was still pale, and sunbaths were given. At 1 year of age, it was noted that he was still markedly pale; the iron ammonium citrate which had been continued for five and a half months was discontinued, and hypo-

Serologic Observations in a Case of Secondary Anemia

Medication.....	2 cc. of liver extract and iron (Lilly no. 55) twice daily, April 9, 1931				
Age ..... Birth Date .....July 25, 1929	19 months March 10, 1931	20 months April 9	21 months April 30	22 months May 21	23 months June 23
Red blood cells.....	3,600,000	3,400,000	5,000,000	5,200,000	5,300,000
Hemoglobin	30%	30%	85%	84%	80% (Tallquist)
White cells	12,300	15,000	14,500	12,900	
Platelets	200,000	240,000	.....	.....	340,000
Polymorphonuclears .	35%	32%	37%	46%	27%
Lymphocytes	57%	63%	56%	43%	69%
Eosinophils	1%	0	1%	2%	1%
Large monocytes	7%	5%	6%	9%	7%
Basophils	0	0	0	0	0
Nucleated red cells....	0	0	0	0	0
Reticulocytes	25%	1%	0.25%	0	0
Infant's weight At birth 1,690 Gm.	9,240 Gm.	9,415 Gm.	10,250 Gm.	10,250 Gm.	10,500 Gm.
Gestation, 33 weeks					
Race, white					
Comment	Marked pallor	Liver extract and iron E. Lilly no. 55 started	Marked improvement in infant's color, etc.		

dermic injections of 1 grain of sodium cacodylate given biweekly were continued for one month. At 13 months the infant suffered another mild attack of diarrhea, and the pallor became more intense. At 14 months of age, liver and other meats were added to the diet, and at 15 months, 1 drachm (3.9 Gm.) of spleen marrow extract was given three times daily after meals. At 19 months of age, the infant showed a lemon yellow pallor; the gums, the lips, the buccal and the conjunctival mucous membranes were markedly pale, as were the beds of the finger-nails and the ear lobes. The spleen was firm and enlarged one fingerbreadth below the costal margin. The appetite was poor, and the infant did not gain well. At 20 months of age, the spleen-marrow extract was discontinued, and liver extract with iron (E. Lilly's, no. 55) was given. In the accompanying table will be noted the complete observations on the blood. In three weeks remarkable improvement was noted, both in the infant's appearance and in the detailed hematologic study.

The liver extract no. 55 with iron used in the treatment of this case (supplied through the courtesy of Eli Lilly & Company) contains liver in the form of dried liver extract, suitable for secondary anemia. This liver fraction is prepared according to the formula of Whipple and Robscheit-Robbins and Walden, and it

is effective in the production of hemoglobin and red cells in dogs made anemic by long-continued bleeding. It contains from 65 to 75 per cent of the potency of whole liver for the production of new hemoglobin in secondary anemia, and represents 3 per cent of the weight of whole liver. This liver fraction should not be confused with the fraction known to be potent in pernicious anemia (no. 343). The latter pernicious anemia fraction contains only from 10 to 20 per cent of the activity of whole liver favoring the production of new hemoglobin in secondary anemia, and therefore, as Minot and Murphy have shown, is relatively inactive in the treatment for secondary anemia.

The iron in this preparation is in the form of ferrous ammonium citrate. Each level teaspoonful (4 cc.) of this liver extract with an iron preparation contains approximately 3.75 Gm. of liver fraction plus 0.65 Gm. (10 grains) of ferrous ammonium citrate. The amount of liver extract contained in one teaspoonful of the preparation has been derived from approximately 125 Gm. of fresh livers.

As has been pointed out, the work of Whipple, Robscheit-Robbins and Walden has demonstrated that a liver fraction which contains from 65 to 70 per cent of the potency of whole liver and probably a number of active substances, and which represents only 3 per cent of the weight of whole liver is an effective therapeutic agent in cases of secondary anemia. Furthermore, they were able to demonstrate experimentally, in dogs, that it was obvious that the effect from the oral administration of iron was more than a mere replacement in the lost or worn-out hemoglobin molecule. They further stated that, "Iron in excess of hemoglobin iron requirements obviously exerts some influence on internal body metabolism," by producing more hemoglobin. This phenomenon they have termed a "salt effect," and it may occur similarly in the feeding of salt mixtures of copper and other metals and ash from liver and kidney.

Finally, it has been found that by feeding liver and iron in combination a "summation effect" is produced, the resulting increase in production of hemoglobin and red cells being the total effect of the organ feeding plus the original value due to the administration of an iron compound alone.

Keefer and Yang reported that an iron preparation and liver given in combination to patients suffering from secondary anemia, especially in anemia due to hookworm infestation, caused improvement more effectively than when either liver or iron was given alone.

The latter observers have noted a definite increase in the percentage of reticulocytes in some of their cases of secondary anemia in which treatment with liver and an iron compound was given. However, the infant presented here showed no increase in reticulated cells.

Recently there have been several favorable reports on the curative effect of iron and copper preparations in the treatment of infants and children with secondary anemia (M. S. Lewis, Hugh Josephs, Leonard Parsons and Helen MacKay). However, I have not noted that so rapid or so marked an improvement has been reported as in this infant.

The combination of an iron and a copper preparation probably produces the salt effect described by Whipple and his co-workers, but the summation effect of liver in combination with iron would seem to be the more rapidly acting and more efficient therapeutic agent.

Book Reviews

Ekzema infantum und Dermatitis seborrhoides. By Dr. Ernst Moro. Paper. Price, 24 marks. Pp. 170, with 125 illustrations. Berlin: Julius Springer, 1932.

This monograph is an elaboration of the author's presentation of the subject to the 1929 Congress of the German Pediatric Society. The first part deals succinctly with the clinical aspects, the seborrheic dermatites, the desquamative erythrodermas and the neurodermites usually classed loosely in the clinic as eczema. The author considers that the multiform types of eczema may all be classed under one of the following four heads: eczema vesiculosum, eczema papulatum, eczema papulovesicolosum and eczema universale of the character of the so-called neurodermatitis disseminata. All these types, as well as crusta lactea (eczema impetiginosum capitis et faciei), which the author considers as a preeczematous dermatosis, are described as they occur in localized or generalized form.

The main part of the work is devoted to pathogenesis. Infantile eczema is considered from the points of view of a neuroreflectory inflammatory process and as a reactive toxic desquamative erythroderma. But it is especially to the consideration of the pathogenesis of eczema as an allergic phenomenon that the author leans. The response of infantile eczema to specific skin allergic tests — the egg-albumin and the Prausnitz-Küstner tests, especially — is particularly stressed by the author. He shows that in eczema over 80 per cent of the patients give a positive reaction to such tests, whereas controls all give negative reactions; those with seborrheic dermatitis give only a very small percentage of positive reactions. The differentiation of eczema from other cutaneous pathologic conditions thereby, especially the seborrheic group, is stressed, and the dependence of certain eczematous characters on sensitization phenomena is also pointed out.

The importance of dietary and metabolic factors, in connection with the consideration of eczema as an allergic manifestation, is a necessary corollary, and the author devotes a chapter to this subject.

The author concludes with comments on the nature of the seborrheic dermatitis and the erythroderma groups.

A word should be said in regard to the numerous and excellent photographic illustrations, which greatly help to explain and clarify the text.

This monograph does much to focus and throw light on many aspects of the newer knowledge bearing on the old vexed question, whether to consider eczema solely as a dermatosis or as a cutaneous manifestation of a systemic derangement the therapeutics of which would be a matter largely for the pediatrician. The full discussion of the sensitization and allergic data given here should pivot the attention of dermatologists to this phase of the subject.

It is hoped that an English translation will appear for the benefit of those who read German with difficulty.

Handbuch der Kinderheilkunde. By Meinhard von Pfaundler and Arthur Schlossmann. Fourth edition. Volume 1. Price, 169 marks. Pp. 1081. Volume 4. Price, 118 marks. Pp. 702. Berlin: Julius Springer, 1931.

Volume 1 of the fourth edition of this well known book has just appeared. Volumes 2 and 3 have already been reviewed in the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**41**:1259 [May] 1931; **42**:498 [Aug.] 1931). Volume 1 is just as well put together and is just as useful as volumes 2 and 3.

The first part of volume 1 takes up general subjects concerning health and disease in childhood, followed by a chapter on "Milk," one on "Breast Feeding" and one on "Metabolism." Then comes a chapter on the "Pathology in the New-Born Period" by von Reuss, with further chapters on "Constitutional Anomalies,"

etc. The chapter on "Rickets and Tetany," by Freudenberg, is especially good and is well illustrated. There follow a chapter on "Scurvy" by Freund, and one on "Diseases of the Blood and Blood Forming Organs" by Opitz. The latter chapter is not as full as one might wish, and the reviewer was unable to find anything about the condition so well known as erythroblastosis, which Cooley so well described. The cuts in this chapter especially the ones in colors, are very good and the pictures are excellent. The volume closes with chapters on the ductless glands.

On the whole, this volume is exceedingly good. It is beautifully illustrated, as are all the other volumes, and is well worth using as a reference book.

Volume 4 takes up "Diseases of the Genito-Urinary Tract," "Diseases of the Nervous System" and "Diseases of the Muscles, Bones and Joints." In this volume the article by Noeggerath on "Genito-Urinary Diseases" is outstanding. However, all the sections are good. "Diseases of the Nervous System" are treated by Ibrahim, and "Psycho-Pathology and Psychoses" by Gött. The illustrations in this work are peculiarly good, and while they are not as elaborate as in some of the other volumes, except in the section on "Genito-Urinary Diseases," they are still well reproduced and excellently suited to illustrate the text.

Psychology and Psychiatry in Pediatrics. The Problem Report of the Subcommittee on Psychology and Psychiatry of the White House Conference on Child Health and Protection, Bronson Crothers, M.D., Chairman. Price, $1.50. Pp. 146. New York: Century Company, 1932.

This report, just published in the series of books sponsored by the White House Conference on Child Health and Protection, considers the important question, should the medical practitioner attempt to give advice when difficulties threaten the satisfactory development of personality in a child under his care? The report is a challenge to pediatricians and family physicians.

Although the report does not urge all physicians to attempt to become expert in the fields of psychology and psychiatry, it states the opinion that adequate physical care of the child cannot be given without attention to whatever intellectual and emotional difficulties may be present, and concludes that when trouble arises and the individual child is in distress a well informed and alert physician is the obvious adviser. "Unwillingness of doctors at large to acquire the ability to deal wisely with problems involving personality of the child," says the report, "may lead to transfer of this field to formal organizations or to individuals without medical experience. Such a solution will inevitably diminish both prestige of the private practitioner of medicine and the interest of his job."

In addition to the body of the report and the discussion, which take up sixty pages, the remainder of the book, with an appendix, consists largely of the report of the Child Guidance Institute in New York and the account of the Essex County Juvenile Clinic in New Jersey. The report of the psychiatry workers is also given, while letters describing typical programs end the volume. This is the most enlightening report on the subject which we have seen.

Child Care and Training. By Marion L. Faegre and J. E. Anderson. Third edition. Price, $2. Pp. 275, with pictures and illustrations. Minneapolis: University of Minnesota Press, 1930.

The authors have attempted to give a complete picture of a growing child. The general principles of child rearing and training are considered, with emphasis on every-day problems.

The subject matter includes both physical and mental development. Physical growth, with weight charts; general care, including diet; clothing; nutrition; infant feeding; posture, and the common children's diseases are considered. There is a discussion of habits: emotional, eating, sleeping, etc. Several chapters are devoted to a discussion of discipline, with constructive suggestions for meeting every-day problems, such as play, curiosity and falsehood.

The psychologic subjects are considered from a conservative, logical standpoint. The authors have not been so successful in their treatment of the physical problems. Such statements as "A healthy child is first of all the proper weight for his age and height" and "By the time children reach the age of six all but three-tenths percent have some defect . . ." are challenged. Statements such as these create an unnecessary overanxiety in the minds of parents, for whom the book was written.

Nutrition Abstract and Reviews. Issued under the direction of the Imperial Agricultural Bureaux Council, Medical Research Council and Reid Library. Volume I. Numbers 1 and 2. Price, 21 shillings per year. Aberdeen: Imperial Bureau of Normal Nutrition, Reid Library, Rowett Institute, Aberdeen University Press, Ltd., 1931.

This is the first number of the abstract journal, which is devoted to abstracts on nutrition and related subjects. The journal has as an introduction an editorial with three short papers on nutrition: "Nutrition and Human Welfare," by Sir Frederick Gowland Hopkins; "Some of the Difficulties in Quantitative Assignment of Human Diets," and "The Qualitative Aspects of Nutrition (with Special Reference to Farm Animals)."

In addition to the pages taken up by these discussions, there are nearly 250 pages of abstracts covering a wide variety of publication.

Courts and Doctors. By Lloyd P. Stryher. Price, $2. Pp. 211. New York: The Macmillan Company, 1932.

The author was for many years general counsel for the Medical Society of the State of New York, and from this experience he has written an interesting book. It contains parts on the relationship of the patients to the physician, the action for malpractice, the defense for malpractice, expert testimony, criminal law and the doctor on the witness stand.

The work is well written and readable. The subject is well put forward and should be of interest to any physician.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.
Place: Geneva, Switzerland. Time: July 15, 1932.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Place: London. Time: 1933.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Jay I. Durand, 1305, 4th Ave., Seattle.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: New Orleans. Time: May 9-13, 1932.

American Academy of Pediatrics

President: Dr. John L. Morse, 319 Longwood Ave., Boston.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New Orleans. Time: May 13-14, 1932.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.
Place: Detroit. Time: September 12-16, 1932.

American Pediatric Society

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Rochester, Minn. Time: May 26-28, 1932.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.
Place New Orleans. Time: May 9-10, 1932.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Kansas City, Mo. Time: Fall, 1932.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. A. Howard Spohn, 925 West Georgia St., Vancouver, B. C.
Secretary: Dr. L. Howard Smith, 734 Medical Arts Bldg., Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Birmingham, Ala. Time: November 16-18, 1932.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.
Place: Mobile. Time: April 19-21, 1932.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Charles E. Boynton, 118 Forrest Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. R. T. Lucas, Shreveport, La.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

MEDICAL SOCIETY OF STATE OF NEW YORK

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester.
Secretary: Dr. Adolph G. G. De Sanctis, 12 E. 11th St., New York.
Place: Buffalo. Time: May, 1932.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. C. E. Bradley, Medical Arts Bldg., Tulsa.
Secretary: Dr. G. H. Harrison, 1200 N. Walker St., Oklahoma City.
Place: Tulsa. Time: May 14, 1932.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

TEXAS PEDIATRIC SOCIETY

President: Dr. J. H. Park, Jr., 3717 Main St., Houston.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Joseph Golomb, 496 E. 17th St., New York.
Secretary: Dr. E. Leonard Benjamin, 2229 Valentine Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Henry E. Irish, 432 S. Lincoln St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Charles Wilson, 10 Peterboro St., Detroit.
Secretary: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: T. Bolling Gay, 384 Peachtree St., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary: Dr. John Caffey, 50 Haven Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Samuel Amberg, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelhia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. C. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 221 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. C. H. Platz, Fort Collins, Colo.
Secretary: Dr. R. H. Verploeg, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William M. Happ, 523 W. 6th St., Los Angeles.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.

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